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ScienceDirect
Magnetic Resonance Imaging 29 (2011) 966–974
MAGNETIC RESONANCE IMAGING

Assessment of pulmonary artery stiffness using velocity-encoding magnetic resonance imaging: evaluation of techniques

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Received 25 September 2010; revised 18 January 2011; accepted 12 April 2011

Abstract

The loss of pulmonary artery (PA) compliance has significant pathophysiological effect on the right ventricle. Noninvasive and reliable assessment of PA wall stiffness would be an essential determiner of right heart load and a clinically useful factor to assess cardiovascular risk. Two MRI techniques have been proposed for assessing PA stiffness by measuring pulse wave velocity (PWV): transit time (TT) and flow area (QA). However, no data are available that compares the two techniques and evaluates their performance, especially over a wide range of PWV values or at 3.0-T, which is the purpose of the present study. Thirty-three patients with different heart conditions were imaged using optimized high-temporal resolution and high-spatial resolution velocity-encoding MRI sequences. Statistical analysis was conducted to study intermethod, interobserver and intraobserver variabilities. The PWV measurements using TT and QA techniques showed good agreement ($P>0.1$). The Bland–Altman analysis showed negligible differences between the two methods (mean±S.D.=0.11±0.35 m/s, correlation coefficient $r=0.94$). The repeated measurements showed low interobserver and intraobserver variabilities, although the S.D. of the differences was larger in the QA technique. The mean±S.D. of the TT/QA measurement differences were −0.05±0.2/0.0±0.36 m/s and 0.02±0.26/0.02±0.39 m/s for the interobserver and intraobserver differences, respectively. In conclusion, each technique has its own advantages and disadvantages. The two techniques result in similar measurements, although the QA method is more subjective due to its dependency on operator intervention.

Keywords: Pulmonary artery; Artery stiffness; Velocity encoding; Pulse wave velocity; Transit time; Flow area

1. Introduction

The pulmonary artery (PA) plays an essential role in smoothing the transition from right ventricular (RV) pulsatile flow to the nearly steady flow at the capillary level [1–3]. In contrast to the systemic arterial system, the pulmonary circulation is a low-pressure, highly distensible system, and the PA branches right away within a few centimeters of the heart. It is helpful to think of the RV and the pulmonary circulation as a coupled unit. The maintenance of this RV–PA coupling is vital to the preservation of right-side heart hemodynamics and of pressure–function association throughout the pulmonary circulation [1,3]. Pulmonary artery compliance is an important factor in decoupling the RV from its vascular load [3,4]. The loss of vascular compliance has considerable pathophysiological relevance, with increased vessel stiffness leading to elevated RV pulsatile workload, decreased contractile performance and augmented energy transmission to smaller pulmonary vessels [1,5]. This functional relation between RV function and PA compliance suggests the importance of PA wall stiffness as an essential determiner of right-side heart load and a clinically useful factor to assess cardiovascular risk [6–8]. Because changes in vascular mechanics can precede gross remodeling, assessment of PA stiffness would enable early identification of many diseases [9–11], e.g., pulmonary arterial hypertension, which is necessary for prompt introduction of targeted therapies. In essence, reliable assessment of PA stiffness may increase understanding of arterial pathophysiology and become a valuable marker for treatment planning and monitoring.

The direct determination of arterial stiffness necessitates the measurement of vessel diameter and pressure. The pressure in the pulmonary circulation can only be measured by

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doi:10.1016/j.mri.2011.04.012

right-side heart catheterization, which is an invasive procedure and thus not well suited for screening or follow-up [12–14]. Assessment of the PA flow can be achieved by a number of methods including electromagnetic tip velocity probe catheters, dye dilution and transesophageal echo-Doppler [15]. Nevertheless, these methods are invasive, may require multiple repetitions and could be harmful. Thus, the need for an accurate and noninvasive method to obtain information about the anatomy and physiology of the PA is of a great importance. A noninvasive method that provides reliable assessment of PA stiffness would be quite useful in clinical practice as well as in research. As radiologic imaging of the heart and the chest is routinely performed in patients with heart and lung disease, noninvasive measurement of PA stiffness from the acquired images means that further information about the patient's condition would be available without levying additional stress on the patient [4,10]. Unfortunately, noninvasive measurements by surface echocardiography are hindered by lack of acoustic window and the difficulty of lining up the beam with the flow direction, particularly in the right and left pulmonary arteries [15]. Furthermore, the accuracy of noninvasive pulse wave velocity (PWV) measurements in the main PA is rather limited due to echo's short penetrating depth [16,17].

Magnetic resonance imaging (MRI) holds promise for the assessment of pathophysiologic conditions in the pulmonary circulation. The ability of MRI to measure flow accurately and obtain high quality anatomical pictures makes this modality widely accepted [12,18,19]. Velocity mapping using phase-encoding MRI is an effective technique for measuring flow in any direction in the heart and arteries [15,20,21]. The feasibility and accuracy of velocity-encoding MRI have been confirmed in normal and pathologic flow conditions and in a number of vascular regions [19,22]. Especially, MRI allows for assessing PA stiffness noninvasively in vivo for the first time by measuring PWV [5]. The measurement of PWV by MRI is helpful in assessing the elastic properties of the PA wall, which in turn may increase understanding of certain vessel pathophysiology [9,23]. Pulse wave velocity is determined by measuring the disturbances in flow or vessel diameter the pressure wave causes [24,25]. Compared with PWV in the aorta, however, PWV in the PA is more difficult to measure and much less documented. The short length of the PA and the reflection waves inflict practical difficulties as high temporal resolution is required [26,27]. Two methods have been proposed for measuring PWV in the PA from MRI images: transit time (TT) [24] and flow area (QA) [16]. The TT method is based on measuring the traveling time the flow wave takes to pass between two sites along the PA with known distance apart. The QA method is based on measuring the incremental change in flow and vessel cross-sectional area during early systole. Limited data are available in the literature on the application of the TT or QA methods for measuring PWV in the PA on a small number of normal volunteers on 1.5-T MRI systems [16,24]. However, no data are available that compare the two methods, especially over a wide range of PWV values or at 3.0-T field strength.

The purpose of the proposed study is to compare the behavior of the TT and QA methods side-by-side for assessing PA stiffness in a group of subjects with wide range of PWV values. The methods will be compared with respect to image acquisition, data analysis and method reliability.

2. Methods

2.1. Study population

Thirty-three volunteers with different heart conditions participated in the study. Table 1 shows more information about the study group diversity, which included ischemic heart disease (n=5), hypertension (n=3), coronary artery disease (n=4), valvular disease (n=5), myocardial infarction (n=4), pulmonary arterial hypertension (n=8) and other conditions (n=4). The study was approved by our internal institutional review board (IRB), and written informed consents were obtained from volunteers before imaging.

2.2. Imaging techniques

All the volunteers were scanned on a 3.0-T Siemens Tim Trio MRI scanner (Siemens Medical Solutions, Erlangen, Germany). Two optimized velocity-encoding cine pulse sequences were applied to each subject. The first pulse sequence was optimized for high temporal resolution to be used in the TT method, while the second pulse sequence was optimized for high spatial resolution to be used in the QA method. The high temporal resolution sequence was implemented twice: at a proximal main pulmonary artery (MPA) cross-sectional location and at either a right pulmonary artery (RPA) or a left pulmonary artery (LPA) distal cross-sectional location, as shown in Fig. 1. The decision to image either the RPA or the LPA was made random in case both branches were well-defined in the scouting images. Otherwise, the branch that appeared better in the scouting images was chosen for imaging. The distance between the two imaging sites (MPA and either RPA or LPA) was about 5 cm. The other (high spatial resolution) sequence was implemented once at the proximal MPA cross-sectional location.

Table 1
Diversity in the study group (mean±S.D.)

Parameter	Mean±S.D.
Sex=19 males and 14 females	
Age (years old)	53±16
Weight (kg)	80±15
Height (cm)	167±9
Heart rate (beats per minute)	68±11
Systolic/diastolic blood pressure (mmHg)	140±14/84±10
Left ventricular ejection fraction (%)	55±11

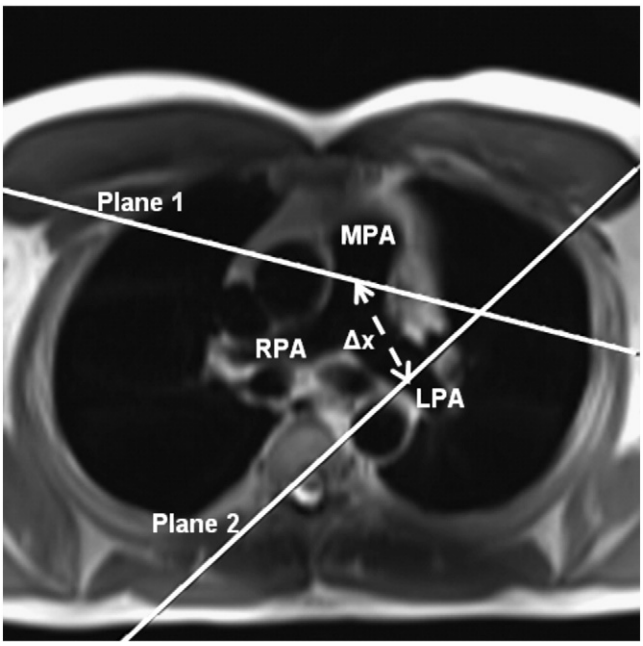

Fig. 1. Planning of the pulmonary flow imaging planes. An axial slice showing the MPA, RPA and LPA, respectively. Two planes are prescribed perpendicular to the flow direction in the PA. Plane 1 is perpendicular to MPA, while plane 2 is perpendicular to LPA. Cine cross-sectional anatomical and velocity-encoding images are acquired at the two planes. The distance along the PA between the two imaging sites is measured (Δx) and used in calculating PWV.

The imaging parameters of the high-temporal resolution imaging sequences were slice thickness=8 mm, TR=7 ms, TE=4 ms, no. averages=1, no. phases=128, velocity encoding=150 cm/s, bandwidth/pixel=340 Hz, flip angle=15°, field of view (FOV)=320 × 320 mm^2, matrix=256 × 256, imaging time ≈2 min (depending on heart rate). The imaging parameters for the high spatial resolution imaging sequence were similar to the high temporal resolution sequence, except for: TR=11 ms, matrix=512 × 512, no. phases=80, imaging time ≈2.5 min (depending on heart rate). In both sequences, velocity encoding was applied in the through-plane direction with white and black representing the maximum velocity (equal to the velocity-encoding value) in the inward and outward directions, respectively. Midgray level represents stationary tissues.

2.3. Image analysis

The images were transferred to a personal computer for off-line analysis with in-house software created in Matlab (MathWorks, Natick, MA). Two modules were designed to measure PWV using the TT and QA methods. In the TT module (Fig. 2), two magnified magnitude images showing the pulmonary cross sections at the two imaging sites were displayed side by side. The operator was asked to mark one point in the center of each cross section. The program then accessed the series of velocity-encoding phase images to calculate the velocity waveforms at these two sites. A 3 × 3-pixels region of interest (ROI) centered at the marked point was used for calculations, where the reported measurement was calculated as the average of velocities inside the ROI. The two velocity curves were displayed together and the program automatically determined the foot-to-foot time interval between the two curves (Δt). The foot of each curve was calculated as the intersection of the up-steeping edge (during early systole) with the baseline velocity. The up-steeping edge was identified as the line connecting the points at the 20% and 80% levels of maximum velocity above the baseline. The baseline was identified as the horizontal line at minimum velocity before the up-steeping edge. Pulse wave velocity was calculated as the ratio of the distance between the two measuring sites along the PA path (Δx) and the traveling time (Δt).

In the QA module (Fig. 3), the series of magnitude images showing magnified view of the PA cross-section at early systole (10–15 slices) were displayed one at a time. For each slice, the operator marked few points along the vessel cross-section boundary. The program then automatically calculated the total area and flow inside the PA cross section from the magnitude and phase images, respectively. The vessel cross-sectional area was calculated as the product of the enclosed number of pixels by the pixel size. Total flow was calculated by adding up the individual flows at all pixels inside the ROI. The measured areas were plotted against flow values during early systole. The operator was asked to confirm the range of valid time frames (for which there is incremental increase in area and flow from timeframe to another). Pulse wave velocity was measured as the slope of the line fitted to the area-flow data (using minimum squared-error principle), which represents the ratio of flow change (ΔQ) and area change (ΔA) during early systole.

2.4. Statistics

The PWV measurements from the TT and QA methods were compared with each other using independent t test. $P<0.001$ was considered significant. Two experts with more than 7 years of experience in cardiac MRI analyzed the images to measure the interobserver variability. One of the experts analyzed the images twice, with 2 weeks in-between to measure intraobserver variability. Bland–Altman [28] and regression analyses were conducted to investigate intermethod, interobserver or intraobserver variabilities. Finally, the measurements from different patient subgroups were recorded, and the PWV values from the pulmonary arterial hypertension patients were compared with those from the rest of the study group.

3. Results

The MRI examination lasted for 15–20 min. Image analysis lasted for about 1 and 4 min for the TT and QA methods, respectively. In two subjects, the PWV measurements by the TT method were obviously wrong (very large

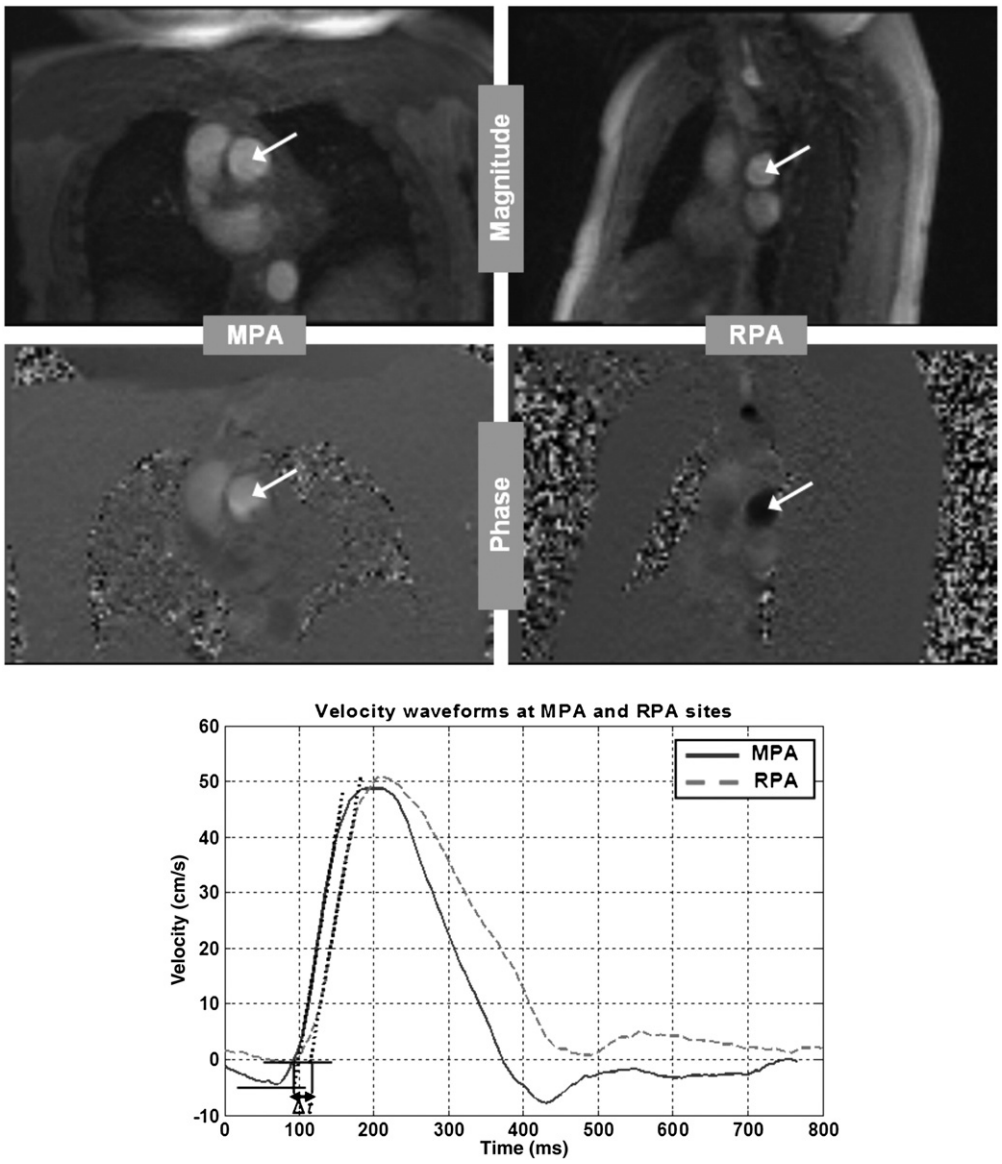

Fig. 2. The TT method for measuring PWV. Anatomical (top) and velocity-encoding (bottom) images showing cross sections of the MPA (left) and RPA (right). The vessel cross sections are pointed to by arrows. The curves (bottom) show the velocity waves in the MPA (solid line) and RPA (dashed line). The TT (Δt) is measured between the curves' feet. The curve foot is determined as the intersection of the baseline velocity (solid horizontal line) and slope of the up-steeping edge (dotted line). Pulse wave velocity is determined as the ratio of the distance between the two measurement sites (Δx) and the TT (Δt).

values). The QA method resulted also in wrong (very large) measurements in another three subjects. These five subjects were excluded from the analysis. For the remaining 28 cases, the PWV measurements by the TT and QA methods showed good agreement (P>0.1). The Bland–Altman plot in Fig. 4 shows mean±S.D. of 0.11±0.35 m/s for the difference between the two methods in estimating PA PWV. All the differences lied within the ±2SD limit. The correlation coefficient between the two methods was r=0.94. The repeated measurements showed low interobserver and intraobserver variabilities, as shown in the Bland–Altman plots in Figs. 5 and 6. The mean±S.D. of the TT/QA measurement differences were −0.05±0.2/0.0±0.36 m/s and 0.02±0.26/0.02±0.39 m/s for the interobserver and intraobserver measurement differences, respectively. The S.D. of the differences between repeated measurements were larger in the QA method than in the TT method (not significant), as shown in Figs. 5 and 6. The TT/QA interobserver and intraobserver correlation coefficients were r=0.97/0.92 and r=0.94/0.91, respectively. The PWV measurements in different patient subgroups are listed in Table 2.The PWV measurements from the pulmonary arterial hypertension group (mean±S.D.=5.2±0.47 m/s, median=5.25 m/s) were significantly (P<0.001) larger than those from the rest of the study group (mean±S.D.=2.8±0.85 m/s, median=2.55 m/s). Next higher PWV values were

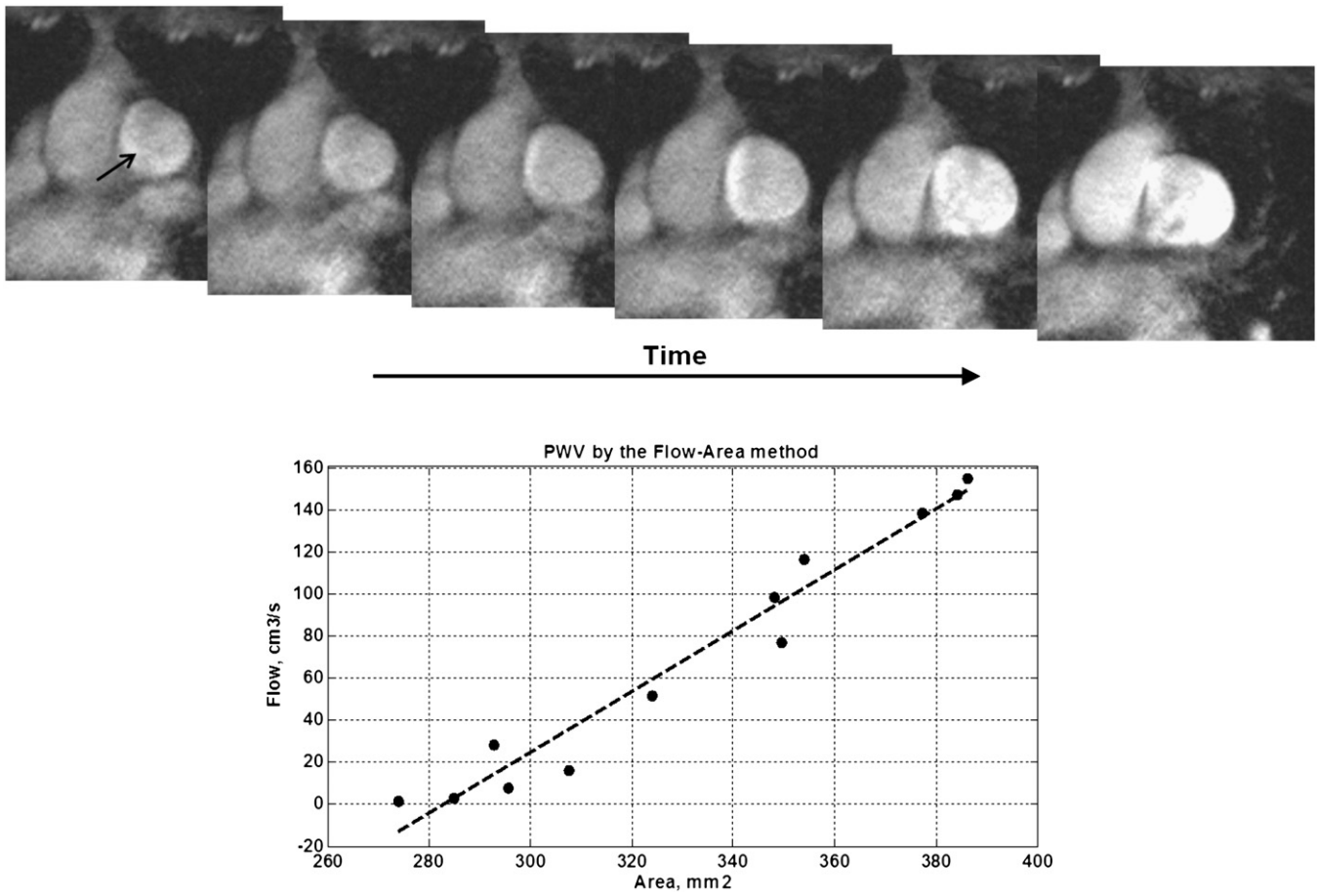

Fig. 3. The QA method for measuring PWV. A succession of cross-sectional images showing MPA (pointed to by an arrow) distending during early systole. The vessel cross-sectional area and flow are measured at each frame during early systole. The plotting in the bottom shows the measured areas versus flow. A line (dashed) is fitted to the measured data, where PWV is determined as the line slope (change in flow over change in area).

recorded in patients with valvular diseases and systemic hypertension, although not significantly different from the average value from all patients.

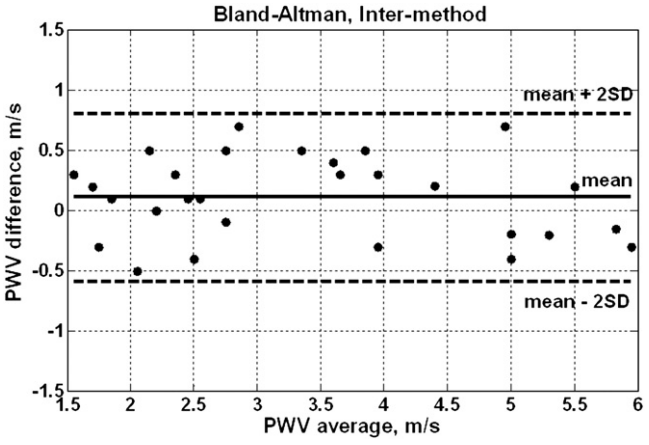

Fig. 4. Bland–Altman plot for the correlation between the TT and QA methods for measuring PWV. All the measurement differences lie between the ±2SD limit, which shows good agreement between the two methods.

4. Discussion

A widely available, noninvasive method for assessing the PA stiffness would be an important advance to identify early disease. Phase-contrast flow MRI is an established technique for noninvasive assessment of hemodynamics that provides two-dimensional maps of flow velocity at the pixel level [19]. An advantage of velocity-encoding MRI over thermodilution catheters is that it is noninvasive and depends less on physiological changes from one cardiac cycle to another (the measurements are averaged over consecutive cardiac cycles) [25]. Assessment of PA stiffness using velocity-encoding MRI can become a noninvasive method to indirectly evaluate different pulmonary diseases. The TT and QA methods have been proposed for measuring PWV in the PA from a series of cine velocity encoding MRI images. However, no studies are available that compare the behavior of the two techniques for measuring PWV in the PA or investigate their reliability, which was the purpose of the proposed study.

The TT and QA techniques showed good agreement in estimating PWV in the PA. They showed failure rates of

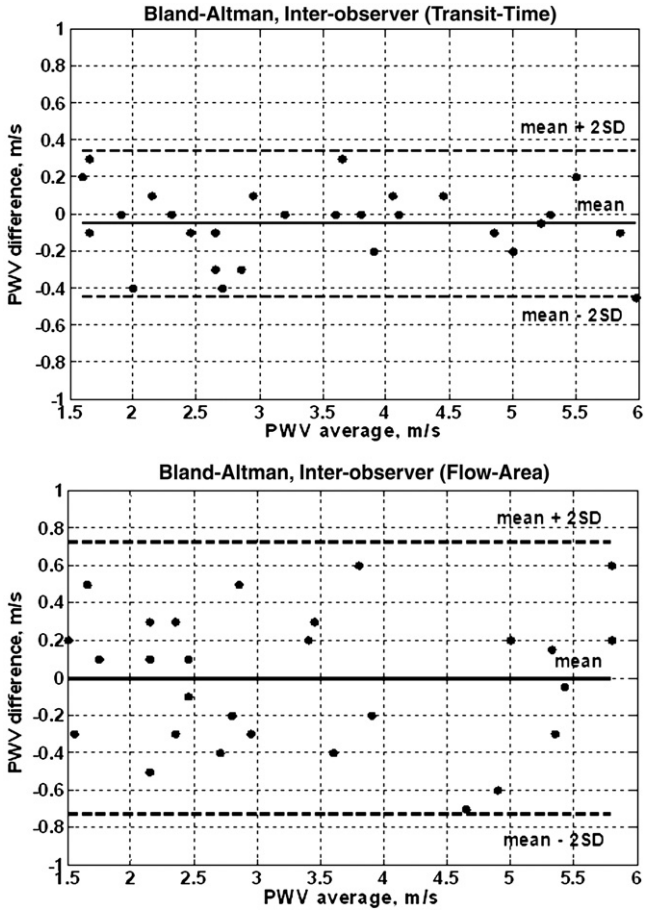

Fig. 5. Bland–Altman plots of interobserver variabilities for the TT (top) and QA (bottom) methods for estimating PWV. The data show low interobserver variabilities, as all measurement differences lie within the ±2SD limit. The QA method shows larger variability (larger S.D. of the differences) than the TT method.

about 7% of all the studied cases. Otherwise, the measurements were similar from the two techniques and were within the range of values reported in the literature [16,24,25]. Due to the short length of the PA, the single-slice QA method seems to be inherently suitable for measuring PWV in the PA. Nevertheless, a long processing time is required, mostly for identifying the vessel cross-section boundary. In the present study, the QA method required four times the processing time required for the TT method. Theoretically, more automated techniques for extracting the PA cross-section, e.g., active contours method [29], should significantly reduce the processing time in the QA method. However, adjacent structures with similar intensity to the PA may result in wrong results, which would then necessitate the operator supervision to review all the frames and correct malidentified boundaries. Another disadvantage of the QA method is its subjective results, which depend on the operator manual selection of the vessel boundary, although this error should be reduced with improved spatial resolution. This effect appeared in the high S.D. associated with repeated QA measurements. It should be noted that, as in the TT method, two measurements at different PA sites could have been used in the QA method. In this case, the final result would be the average of the two PWV values. However, despite expected improvement in accuracy, this criterion would double the imaging and processing times, making the method impractical.

The TT method, on the other hand, has some limitations. The method requires double the imaging time as in the QA method due to the acquisition of two slices separated by a certain distance. Although the sequence used in this study resulted in satisfactory temporal resolution, other techniques could be applied to increase the temporal resolution, though at the expense of increased scan time and patient discomfort. For example repeating data acquisition with trigger delay set to half the imaging sequence repetition time would double the temporal resolution when the data from the two scans are interleaved. However, this technique doubles the scan time as well and may result in compromised results due to different physiological parameters between the two scans.

The use of a 3.0-T scanner in this study allowed for improving the temporal and spatial resolutions in the TT and

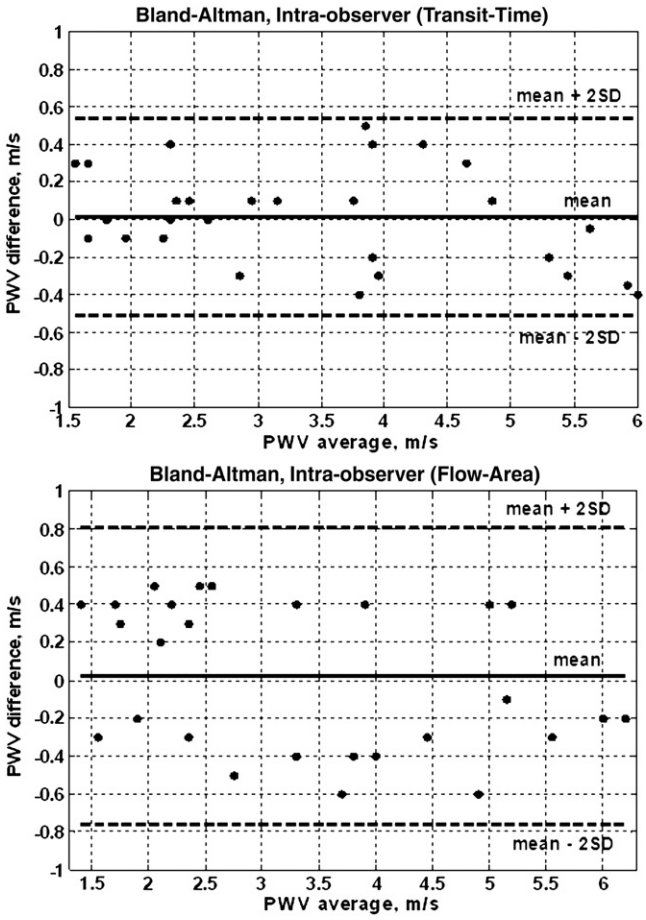

Fig. 6. Bland–Altman plots of intraobserver variabilities for the TT (top) and QA (bottom) methods for estimating PWV. The data show low intraobserver variabilities, as all measurement differences lie within the ±2SD limit. The QA method shows larger variability (larger S.D. of the differences) than the TT method.

Table 2
Pulse wave velocity measurements in different patient subgroups (mean±S.D. in ms)

Disease	*n*	Mean±S.D.
Ischemic heart disease	4	2.3±0.9
Hypertension	3	2.8±0.7
Coronary artery disease	4	2.6±0.8
Valvular disease	4	3.5±0.5
Myocardium infarction	4	2.4±0.9
Pulmonary arterial hypertension	8	5.2±0.5

QA sequences, respectively. Basically, the 3.0-T field doubles the signal-to-noise ratio (SNR) compared with standard 1.5-T machines. The gain in SNR can then be traded for improved temporal or spatial resolutions, as needed. Although the present study is not intended to compare results from 1.5 and 3.0 T, the achieved temporal and spatial resolutions were superior to results from 1.5-T machines [16,24]. This should have contributed to the reproducible results shown in the Results section.

In this study, two pulse sequences were used and separately optimized for the TT and QA methods. While only one sequence with compromised temporal and spatial resolutions could have been designed for the two methods, this may have resulted in marginal performance of both techniques, which would confound a fair comparison between them. The velocity-encoding value of 150 cm/s used in this study was sufficient in all the cases. A lower value of 120 cm/s would have resulted in aliasing in some of the cases when the flow velocity exceeded 120 cm/s. On the other hand, larger velocity-encoding values are not recommended as they reduce the method sensitivity.

Although the number of subjects with pulmonary disease, e.g., pulmonary arterial hypertension, analyzed in this study was limited, these initial results suggest a role of PWV measured by MRI in revealing altered vascular dynamics in the pulmonary circulation. In the present study, the feasibility and comparison of different techniques for measuring PA PWV have been investigated over a wide range of PWV values. While the study was not intended to investigate the differences between PWV values in different heart conditions, the results in Table 2 suggests that PWV measurements tend to be slightly different depending on the patient group studied. The results also showed that patients with pulmonary arterial hypertension, which significantly alters the PA vessel wall structure, had significantly higher PWV values than the rest of the study group, as shown in the Results section. These encouraging results, together with the potential of MRI for hemodynamic measurements, should be confirmed in a larger study that targets only patients with pulmonary disease.

4.1. Study limitations

The proposed methods have some limitations that may lead to their inapplicability in certain cases, as shown in the Results section and as previously discussed in other articles [16,24]. The source of error in the QA method is that the vessel cross-section position might move significantly in the slice plane between end diastole and end systole due to whole heart contraction and probably due to individual PA shapes as well [30], as shown in Fig. 7. This results in negligible change in the vessel cross-sectional area during early systole, which in turn, results in wrong (very large) PWV values. The limitation of the TT method is that the curved nature of the PA path and the individual anatomical variation may make it difficult to establish a standardized scouting method for determining the PA cross-sectional slices, which thus requires an experienced scanner operator. In patients with short PA path, the TT analysis may result in negligible traveling time of the flow wave between the two measurement sites, which leads to erroneous results (Fig. 8), although this source of error should be minimized with high temporal resolution. It should be noted that despite the erroneous results in some of the studied cases, the proposed methods showed successful application in 93% of the analyzed cases. The few cases that showed errors were easily identified from the analysis curves, e.g., no change in

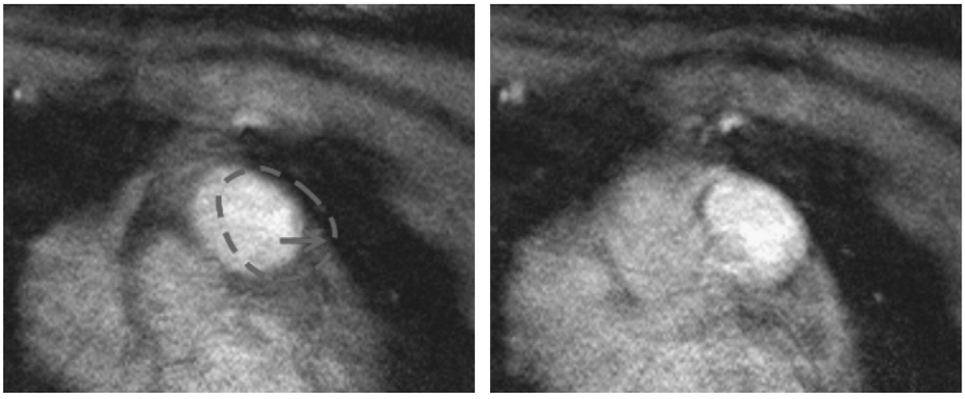

Fig. 7. Pulmonary artery movement during the cardiac cycle. The MPA moves with the heart during systole. The slices on the left and right show the vessel cross-section position at early systole and end systole, respectively. The end-systolic position was drawn as a dashed contour on the left slice, which shows a significant vessel movement that affects accurate measurement of pulmonary cross-sectional area, necessary for calculating PWV in the QA method.

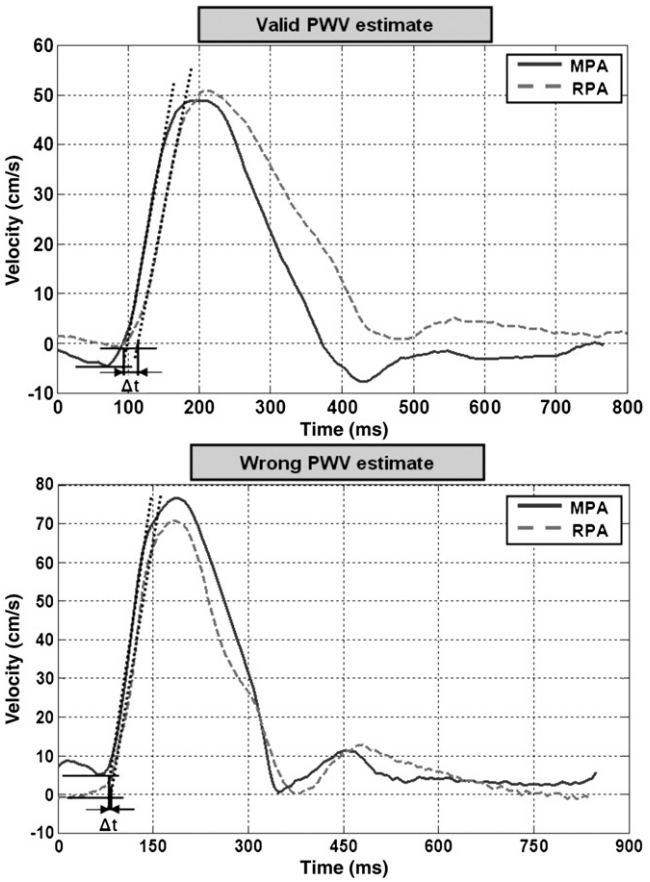

Fig. 8. Errors in estimating PWV using the TT method. The plots show velocity waves measured at the main and right pulmonary arteries cross sections. The case in the top results in a correct assessment of the TT (Δt), which leads to a valid PWV measurement, while the case in the bottom shows negligible TT, which results in a very large and incorrect PWV estimate.

the PA cross sectional area during systole in the QA method, or zero traveling time between the two flow waves in the TT method. For all analyzed patients, at least one of the two proposed techniques worked successfully, which suggests that the appropriate analysis method should be selected based on individual patient anatomy, i.e., apply the QA method when PA path is very short and apply the TT method when the PA position changes significantly during the cardiac cycle, which can be easily judged after a quick review of the acquired cine scouting images.

5. Conclusion

The TT and QA methods are noninvasive and feasible techniques for measuring PWV in the PA. The two methods result in similar PWV measurements, although the QA method is more subjective due to its dependency on operator intervention. Each technique has its own advantages and disadvantages. The TT method requires high temporal resolution and long imaging time and is preferable if plane scouting of the PA cross-sectional slices is not complicated. On the other hand, the QA method is preferable in difficult patients, although it requires high spatial resolution and long processing time.

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