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Slice Location Dependence of Aortic Regurgitation Measurements with MR Phase Velocity Mapping

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George P. Chatzimavroudis, Peter G. Walker, John N. Oshinski, Robert H. Franch, Roderic I. Pettigrew, Ajit P. Yoganathan

Although several methods have been used clinically to assess aortic regurgitation (AR), there is no "gold standard" for regurgitant volume measurement. Magnetic resonance phase velocity mapping (PVM) can be used for noninvasive blood flow measurements. To evaluate the accuracy of PVM in quantifying AR with a single imaging slice in the ascending aorta, *in vitro* experiments were performed by using a compliant aortic model. Attention was focused on determining the slice location that provided the best results. The most accurate measurements were taken between the aortic valve annulus and the coronary ostia where the measured (Y) and actual (X) flow rate had close agreement ($Y = 0.954 \times X + 0.126$, $r^2 = 0.995$, standard deviation of error = 0.139 L/min). Beyond the coronary ostia, coronary flow and aortic compliance negatively affected the accuracy of the measurements. *In vivo* measurements taken on patients with AR showed the same tendency with the *in vitro* results. In making decisions regarding patient treatment, diagnostic accuracy is very important. The results from this study suggest that higher accuracy is achieved by placing the slice between the aortic valve and the coronary ostia and that this is the region where attention should be focused for further clinical investigation.

Key words: aortic regurgitation; regurgitant volume; magnetic resonance phase velocity mapping; aortic compliance.

INTRODUCTION

Chronic aortic regurgitation (AR) leads to left ventricular dysfunction which, if untreated, can cause death. Knowledge of the severity of the disease is important, because it is used to guide patient management and to determine timing for valve replacement surgery.

Traditional methods, such as angiography (1), have been used to quantify AR, but they are invasive and semi-quantitative at best. A number of invasive and non-invasive echocardiographic techniques (2–5) were investigated to assess AR, with only qualitative results. Color Doppler echocardiography and magnetic resonance im-

aging (MRI) studies related the geometrical parameters of the regurgitant jet in the left ventricle (LV) with the severity of AR (6–11), but the results correlated only fairly with angiographic grading data. Generally, technical limitations make these techniques unsatisfactory and, in addition, no direct value for the aortic regurgitant volume (ARV) can be determined. MRI volumetric studies (11–13) tried to measure the ARV as a difference between the left and right ventricular stroke volumes, but this approach is not valid in the simultaneous presence of regurgitation of other heart valves. Another clinical method, the proximal isovelocity surface area (PISA) method (14) is not applicable to the measurement of AR, because it is affected by the geometry of the valve (15) and the confinement by the walls of the aorta (16). Therefore, there is still a need for a reliable method to accurately quantify AR.

Magnetic resonance phase velocity mapping (PVM) is a technique capable of providing accurate blood velocity measurements (17–19). By positioning an imaging slice perpendicular to the long axis of a vessel, blood velocity through that slice can be measured over the entire cross-sectional area of the vessel and then the instantaneous flow rate and the volume over any specified period of time can be calculated. PVM has been used to measure the ARV *in vivo* (13, 20–22) with promising results. However, each study involved different measurement protocols, with different slice locations and imaging parameters. One should note that, if the imaging slice is located in the ascending aorta superior to the sinotubular junction, the regurgitant flow includes the coronary flow. At the same time, because of aortic compliance, there will be a decrease of the aortic diameter during diastole forcing some blood to flow towards the valve, that will never pass through the slice, and the rest of blood to flow through the slice, but in the forward direction towards the systemic circulation. This will cause an underestimation of the regurgitant flow rate. A possible solution could be to place the slice in the vicinity of the aortic valve. There, however, the more complex flow environment could affect the accuracy of PVM measurements. The effects of these factors on the accuracy of the ARV measurements have not been investigated. Since there is no other reliable *in vivo* quantitative method for measuring AR, the accuracy of the PVM technique must be examined in an *in vitro* environment, using a model with a geometry similar to the anatomical, where the flow rates can be easily controlled and measured. Furthermore, the factors under investigation can be studied separately or in combination and much stronger conclusions regarding their effects can be drawn.

The aim of this study was to investigate, in an *in vitro* environment, how accurate magnetic resonance phase velocity mapping is in quantifying the aortic regurgitant volume, and to study the effects of coronary flow, aortic compliance and velocity field on this accuracy. In addition, preliminary measurements *in vivo* were taken to better evaluate the *in vitro* results.

METHODS

In Vitro Measurements

A straight silicone model of the ascending aorta, with a stentless porcine aortic valve, the sinuses of Valsalva and two Tygon tubes (3 mm ID) representing the coronary arteries, were used for *in vitro* measurements (Fig. 1). Regurgitation was created by placing plastic cylindrical tubes between the leaflets of the valve to prevent complete closure. Water was used as the blood analog fluid in all experiments for simplicity, although its viscosity is approximately 3.5 times lower than that of blood, since, in the aortic root, flow is predominantly driven by inertia compared with viscous mechanisms. The model was mounted in a large water-filled container to provide a stronger MR signal.

To investigate the effect of coronary artery flow on the ARV measurements, the model was placed in a steady flow loop. The direction of the flow was similar to that of a regurgitant flow, i.e., from the aorta to the LV. The regurgitant flow rate was measured with a rotameter and the coronary flow rate by timing the filling of a graduated cylinder. The entire system was placed in a 1.5 Tesla scanner (ACS Gyroscan, Philips Medical Systems, Shelton, CT). Initially, a coronal scout spin-echo image was acquired [slice thickness (ST): 7 mm; field of view (FOV): 300 mm; echo time (TE): 25 ms; repetition time (TR): 432 ms; matrix size: 256 × 256]. A number of transverse, gradient-echo, velocity-encoded images were taken at four locations: (i) at the valve annulus level; (ii) between the valve annulus and the coronary ostia (0.5 cm from the

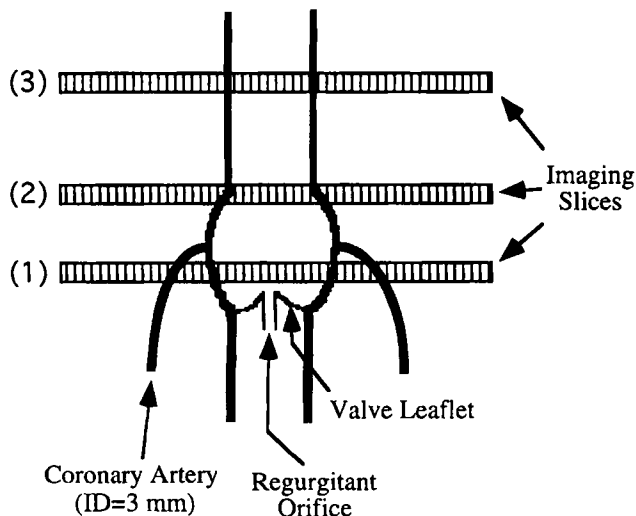


FIG. 1. Aortic root model. Three slice locations are shown: between the valve and the coronary ostia (1); at the sinotubular junction (2); and in the ascending aorta (3).

valve) or at Location 1 in Fig. 1; (iii) at the sinotubular junction (2.0 cm from the valve) or at Location 2 in Fig. 1; and (iv) beyond the sinotubular junction (4.0 cm from the valve) or at Location 3 in Fig. 1. A range of regurgitant orifice diameters (1, 3, and 5 mm) and orifice velocities (2–5 m/s) were used to cover the clinical range of severity of AR. As a result, a range of regurgitant flow rates from 0.1 to 5.5 L/min were used. A range of velocity encoding values (25–500 cm/s) was used depending on slice location. The coronary artery flow rate was 0.3 L/min. For each acquisition (ST: 5 mm; FOV: 200 mm; TR: 30 ms; TE: 6–9 ms; Flip angle: 35°; matrix size: 128 × 128; pixel size: 1.56 × 1.56 mm), a modulus and a phase image were acquired (Figs. 2a and 2b).

To investigate the effect of aortic compliance on the ARV measurements, pulsatile flow was generated by a computer-controlled piston pump (SuperPump, SPS 3891 Vivitro Systems Inc., Victoria, British Columbia, Canada) by using the same aortic model. No coronary flow was allowed to focus on the compliance effect. The aortic flow rate was measured with a brass transit time ultrasonic flow probe (24N in-line, Transonic Systems Inc., Ithaca, NY), located next to the valve in the LV side, by using a single channel flowmeter (T-108, Transonic Systems Inc.). The flow waveform was recorded on a Macintosh IICI computer by digitizing the analog signal from the flowmeter with an A/D board (NB-MIO-16, National Instruments Inc., Austin, TX) and using the LabVIEW software (Version 3.0, National Instruments, Inc.). After the coronal scout image was acquired by using ECG triggering, the velocity-encoded transverse images were taken at three locations: (i) 0.5 cm from the valve (corresponding to the region between the valve annulus and the coronary ostia), Location 1; (ii) 2.0 cm from the valve (sinotubular junction), Location 2; and (iii) 4.0 cm from the valve, Location 3. A range of degrees of severity of AR was produced (ARV = 7–75 ml/beat) by using four regurgitant orifices (2, 3, 4, and 5 mm in diameter). The change in aortic diameter between systole and diastole in normal cases is 10–15% (23), but it can be outside of this range, depending on factors such as age or the pathological state (24) of the aortic wall. In these experiments, the diameter change was varied between 10% and 50% to obtain more complete results. The total output of the piston pump was 4.2 L/min with a cycle rate of 60 beats/min. Retrospective ECG gating was used to acquire 20 frames per cycle (same imaging parameters as in steady flow).

In Vivo Measurements

To evaluate the *in vitro* results clinically, measurements were taken on five normal volunteers and three patients with AR [moderate-to-severe (Grade 3) as assessed by angiography and echocardiography]. After the aortic root was located in the spin-echo scout image (Fig. 3a), an LVOT gradient-echo cine scout acquisition (TR: 30 ms; TE: 6 ms; FOV: 250 mm; ST: 5 mm) was taken to provide additional information about the valve and the coronary ostia (Fig. 3b). On these images, the valve was located from direct visualization of the valve leaflets or from a dark area (reduced signal) just proximal to the regurgitant

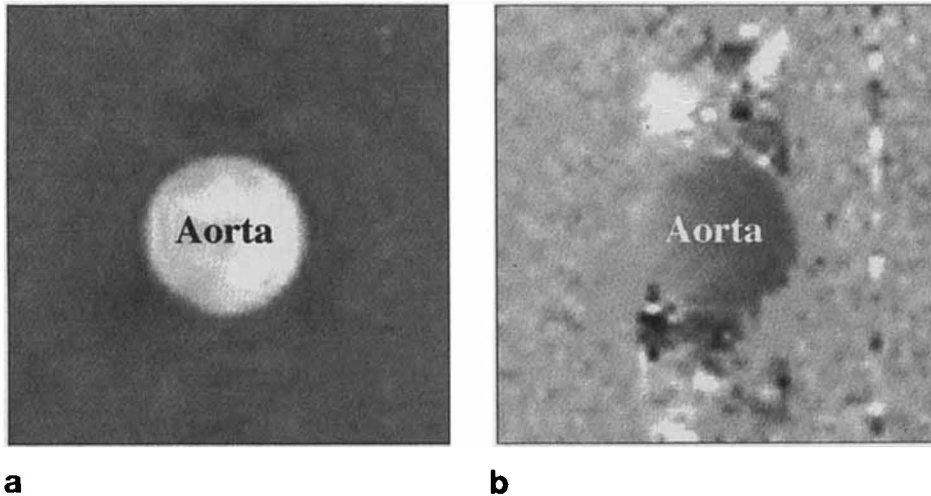


FIG. 2. (a) Modulus and (b) phase transverse gradient-echo images (FOV: 200 mm; ST: 5 mm; TR: 30 ms; TE: 8 ms; matrix size: 128 × 128; retrospective ECG cardiac gating; 20 phases; 2 signals averaged).

orifice caused by flow acceleration. Also, the origins of the coronary arteries were seen by combining the scouts and were used as a guide for the location of the slice between the valve annulus and the coronary ostia. Similar to the *in vitro* protocol, measurements were taken perpendicular to the long axis of the aorta in three locations (Fig. 3a): (i) between the valve annulus and the coronary ostia; (ii) at the sinotubular junction; and (iii) 2 cm beyond the sinotubular junction. The velocity encoding value used was varied (50–200 cm/s) depending on slice location. Each velocity-encoded acquisition required approximately 4 min, depending on the heart rate of the volunteer.

Image And Data Analysis

The phase images were initially processed to remove the phase offset due to eddy currents. Pixels of stationary tissue should have phase values corresponding to zero velocity. Based on that, an “error image” was created for each phase image. In this “error image,” each pixel represented the phase offset value for the corresponding pixel in the initial phase image (“errors” for all pixels were determined through 2D regression analysis using, as data, the phase offset values from the stationary tissue pixels). Thus, a set of “error images” was created and, by subtracting each of them from the corresponding initial phase image, pixel by pixel, a new corrected phase image was created (25). The cross-section of the aorta was identified and selected on each modulus image of the cycle separately (based on the higher signal intensity of flowing blood in the aorta) and the selection was applied to the phase images. The phase was converted to velocity, based on the linearity between MR signal phase and velocity, and integration of this velocity over the cross-sectional area of the aorta yielded the flow rate. Then, the ARV was calculated by integrating the instantaneous regurgitant flow rate curve over diastole. Also, from the modulus images, the change in the cross-sectional area of the aorta was observed throughout the cardiac cycle. By knowing the aortic cross-sectional area change at the

slice Locations 1, 2, and 3 (Fig. 1), the volume change between these locations was determined. These direct measured volume changes were compared with the change in the regurgitant volume measured with PVM at the same locations to investigate more quantitatively the effect of compliance.

Statistical Analysis

A sign test was applied to determine if there was a significant difference in the regurgitant flow rates between measurements at different locations. The sign test was used because the number of data in each case was small for application of the *t* test. Flowrates were normalized with respect to the actual regurgitant flow rates. Interobserver variability was studied by separate analysis of the images by two investigators who were blinded to one another's analysis. Regression analysis and a sign test were applied to determine the degree of the reproducibility.

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RESULTS

In Vitro

Figure 4 shows the measured regurgitant flow rates between the valve and the coronary ostia (Location 1). The measured flow rate excluded the coronary flow, thus giving the actual regurgitant flow rate. This is seen from the data points that tend to fall on the solid line representing the regurgitant flow rate and from the regression line where the slope is essentially 1.0 and the intercept is small. However, when the slice was placed at the sinotubular junction (Location 2), the measured flow rate included the coronary flow. This was observed from the data points falling on the dashed line representing the combined (regurgitant plus coronary) flow rate and from the regression equation [$y = 0.995x + 0.338$, $r^2 = 0.995$, standard deviation of error (SDE) = 0.152 L/min], where the slope was essentially 1.0 and the intercept was approximately 0.3 L/min (coronary flow rate). Similar results were observed for measurements taken beyond the sinotubular junction (location 3: $y = 0.984x + 0.286$, $r^2 = 0.998$, SDE = 0.077 L/min). A sign test showed that there was a significant difference when the measurements between the valve annulus and the coronary ostia were compared with those at the sinotubular junction or beyond it ($P < 0.05$). No significant difference was found between the measured flow rates at Location 1 and the actual regurgitant flow rates ($P = 0.18$). There was no significant difference between the measurements at slice Locations 2 and 3 ($P = 0.18$) which, in addition, were significantly different to the actual regurgitant flow rate ($P < 0.005$). PVM measurements at the valve annulus

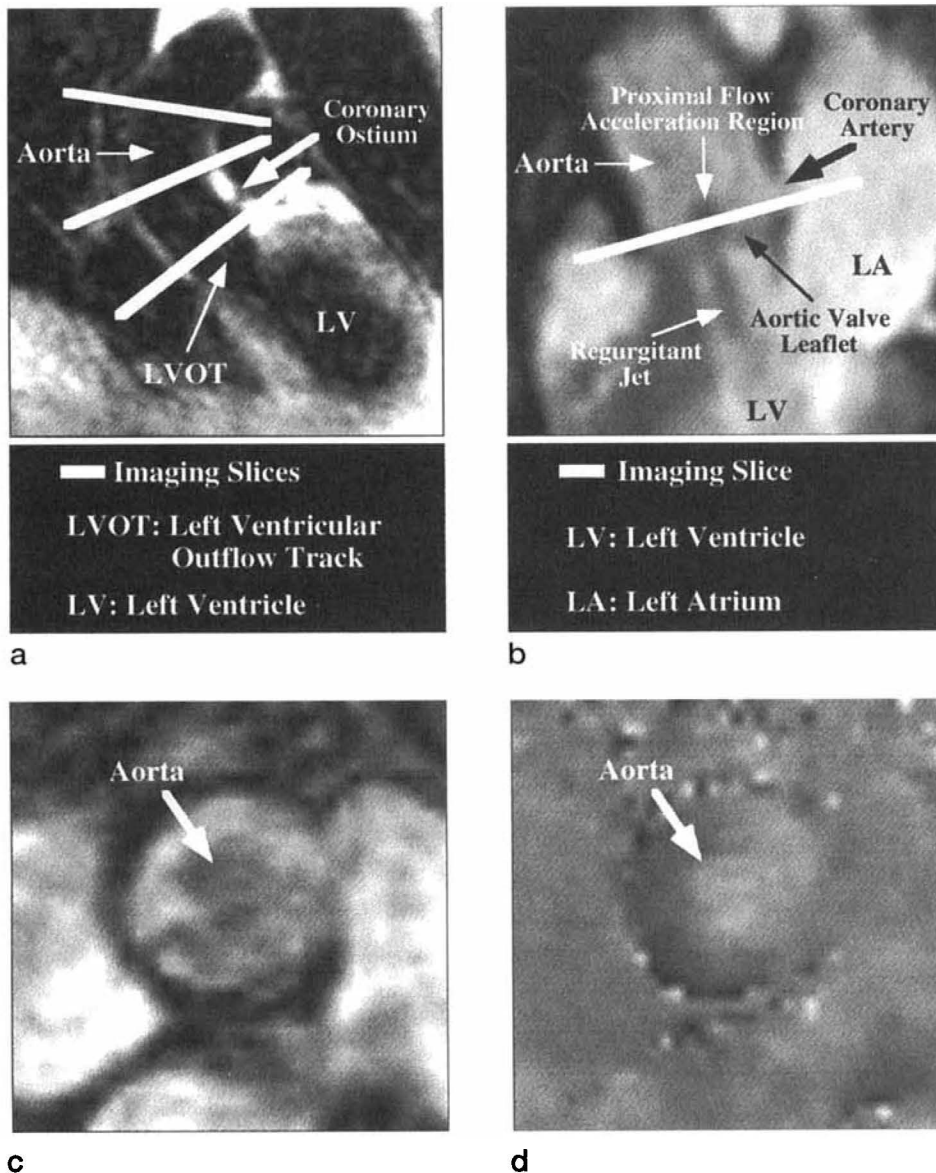


FIG. 3. (a) Spin-echo coronal scout image and slice locations: between the valve and the coronary ostia (1); at the sinotubular junction (2); and in the ascending aorta (3) (FOV: 300 mm; ST: 7 mm; TR: 432 ms; TE: 25 ms; 2 signals averaged). The aortic root and coronary ostium are seen. (b) LVOT gradient-echo image to locate the valve and coronary ostia (FOV: 250 mm; ST: 5 mm; TR: 30 ms; TE: 6 ms; flip angle: 30°; 2 signals averaged). (c) modulus and (d) phase images acquired in the aortic root (FOV: 200 mm; ST: 5 mm; TR: 30 ms; TE: 6 ms; flip angle: 35°; retrospective gating; 2 signals averaged). The aorta is clearly distinguished.

level were not accurate ($y = 0.455x + 0.191$, $r^2 = 0.31$, $SDE = 1.361$ L/min).

Figure 5 shows the change in the measured ARV as the distance between the slice and the valve annulus increases, in the case of 35, 40, and 45 ml/beat actual ARV (moderate-to-severe). At 0.5 cm from the valve, the measurements were very accurate. However, there was a decrease in the measured ARVs as the distance of the slice from the valve increased. This behavior was observed for the entire set of ARVs used in the experiments. The average error in the measurements (based on the actual ARV) at slice Location 1 was approximately 2%. This error increased as the distance of the slice from the

valve annulus increased. Hence, for slice Location 2, this error was approximately 12% and for slice Location 3, it was approximately 22%. As seen in Fig. 6, the aortic volume change during the cardiac cycle between slice Locations 1 and 2 or between Locations 2 and 3, as measured directly from the modulus images, was well related to the difference in the measured ARV between those specific locations ($y = 1.1079x - 0.0661$, $r^2 = 0.87$).

In Vivo

No significant ARV was measured in any of the healthy volunteers (<2 ml/beat). In the case of the patients, there was a decrease in the measured ARV as the slice was moved away from the valve in the ascending aorta (Fig. 7).

The interobserver variability of the regurgitant volume calculations was found to be very small by simple regression analysis on the calculated ARVs ($y = 1.050x - 0.441$, $r^2 = 0.998$, $SDE = 0.782$ ml, $P < 0.001$, where y : Reviewer 1 and x : Reviewer 2). Also, a sign test showed that there was no significant difference between the results of the two separate analyses ($P = 0.11$).

DISCUSSION

Although recent studies have shown that the single slice PVM technique has great potential for quantifying AR, determining the proper measurement location is of great

importance in the clinical establishment of the technique. This depends, first of all, on understanding the effects of fluid mechanics factors on the PVM results.

When the slice was placed above the coronary ostia, the measurement of the regurgitant flow included the coronary flow, resulting in an overestimation of the severity of regurgitation. However, coronary flow is generally small (2–4 ml/beat) and its effect on the measurement of the regurgitant volume is, therefore, small in cases of moderate and severe AR. For example, if the actual regurgitant volume is 30 ml/beat, the measured regurgitant volume at the sinotubular junction, could be 34 ml/beat considering a coronary flow of 4 ml/beat,

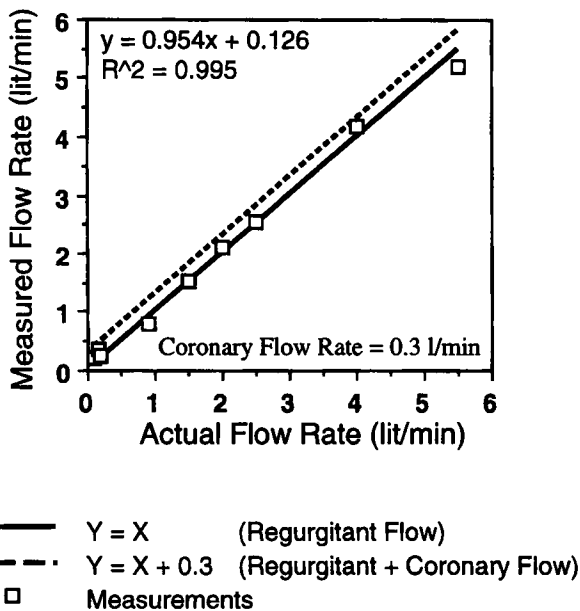


FIG. 4. Steady flow results. Imaging slice located 0.5 cm from valve annulus (between coronary ostia and valve).

leading to a relatively small error of 13%. This will not be the case in milder AR cases. For an actual regurgitant volume of 10 ml/beat, the measured regurgitant volume at the sinotubular junction, could be as high as 14 ml/beat, leading to a 40% error.

The observed decrease in the measured ARV as the slice location was moved cranially away from the aortic valve shows the effect of aortic compliance. Measurements taken between the valve annulus and the coronary ostia were accurate whereas the errors in the measured ARV increased with the distance of the slice from the valve (>20%). To obtain a more quantitative sense of the compliance effect, the change in the measured ARV between two different slice locations was compared with the aortic volume change, in diastole, between the same

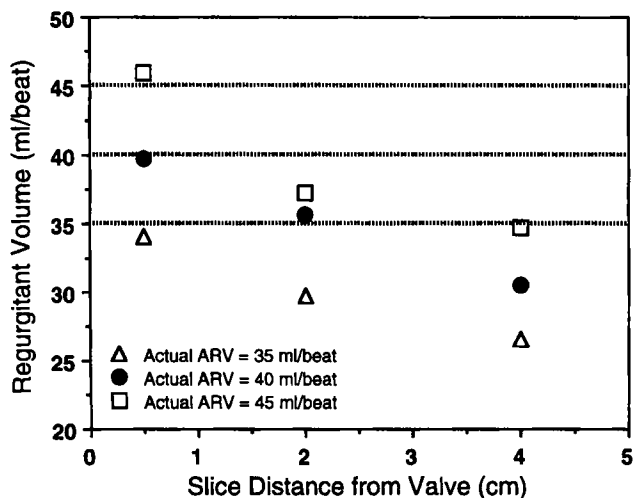


FIG. 5. Pulsatile flow results. Measured regurgitant volume at 0.5, 2, and 4 cm from the valve annulus for three different aortic regurgitant volumes: 35, 40, and 45 ml/beat (moderate-to-severe AR).

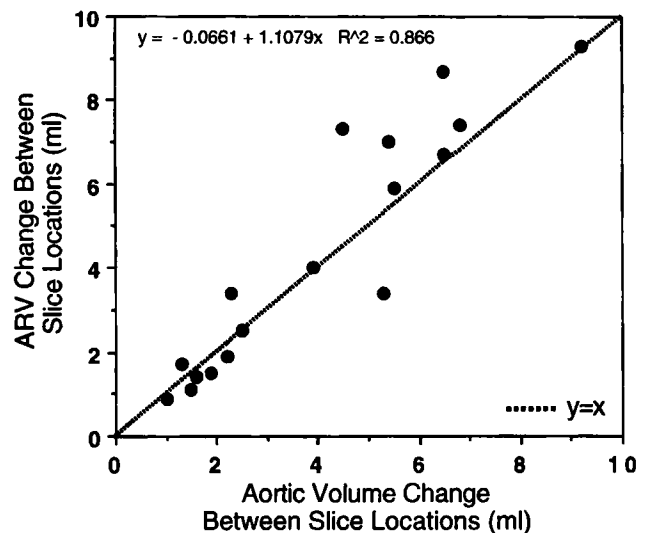


FIG. 6. Aortic volume change during the cardiac cycle (as measured directly from the images) between slice Locations 1 and 2 or 2 and 3 (see Fig. 1) versus ARV difference between these locations as measured with PVM. A range of aortic diameter changes (between 10 and 50%) was used during the experiments resulting in a range of aortic volume changes.

two locations. A good correlation was observed (Fig. 6), indicating the importance of compliance.

Similar to the *in vitro* results, the preliminary *in vivo* measurements showed a decrease in the measured ARV with distance from the valve due to compliance. The accuracy of the *in vivo* measurements cannot be validated, due to the lack of any other reliable quantitative clinical method. However, the agreement in the tendency between *in vitro* and *in vivo* data is a strong indication of the importance of the *in vitro* results and suggests that, to

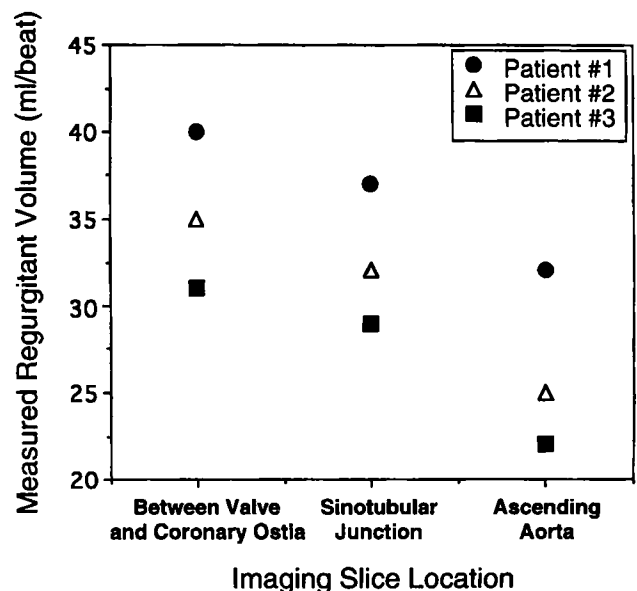


FIG. 7. Measured regurgitant volume on three patients with moderate-to-severe AR: Note the decrease in ARV as the slice location is moved away from the valve annulus.

avoid errors, the proper slice location is between the valve annulus and the coronary ostia.

By moving the slice close to the regurgitant orifice, of consideration was the effect of flow field in that region. Generally, large convective acceleration can lead to considerable velocity errors (26) and misregistrations of the exact location of measurement (26, 27) when using PVM. Nevertheless, the present results between the valve and the coronary ostia are accurate. One should note that the measurements were not taken too close to the valvular level (where the slice would be in a region of too rapid acceleration). Therefore, the results should not be significantly affected since, in addition, short *TEs* (6–9 ms in this study) were used. Use of short *TEs* prevents dephasing of the MR signal in regions of accelerating and, generally, complex flow and allow reliable measurements of blood velocity. In the present study, with the help of the LVOT cine set of images, the measurements between the valve annulus and the coronary ostia were taken so that the 5-mm thick slice would be as far as possible from the regurgitant orifice, regardless of any aortic motion in the *in vivo* cases. Although, some acceleration of flow was present (recognized by a hemispherically shaped reduced-signal area at the tip of the valve leaflets in the LVOT scout image during diastole, see Fig. 3b), the velocity information was not lost or significantly distorted.

Both *in vitro* and *in vivo* measurements at the valve level provided unreliable results. In addition, the quality of the images at the valvular level was unsatisfactory, making the analysis more unreliable. Use of extra-short *TEs* (<4 ms) has been reported to partially reduce the problem of signal loss and signal phase distortion due to very large acceleration and turbulence (28, 29). However, the shorter the *TE*, the lower the signal-to-noise ratio due to hardware limitations, and this causes uncertainties and possible errors in the calculation of the flow rate through the orifice. In addition, partial volume effects and proper slice thickness selection are important factors in the accuracy of the regurgitant measurements. Generally, good quality images make the analysis more objective. The images from the *in vivo* measurements close to the valve were of good quality and can provide a reliable diagnosis.

This MR technique is based on the principle of mass conservation. Based on that principle, flow through the imaging slice will pass through the regurgitant orifice (since the effects of coronary flow and aortic compliance are eliminated if the imaging slice is placed close to the valve). The same principle is taken into account in the control volume concept, introduced in a previous study by Walker *et al.* (19), where, after acquiring a number of contiguous images in the region of a regurgitant orifice, and measuring all three velocity components, an imaginary cubical control volume encompassing the orifice was constructed to quantify the regurgitant flow. Although this approach is very promising for the quantification of mitral regurgitation, it is time consuming with conventional imaging techniques. Furthermore, the geometry of the aortic root could complicate its implementation in the case of AR. In addition, situations of perivalvular leakage can be reliably diagnosed by a single slice measurement, in contrast to the multislice control

volume method. Another important advantage of the single slice technique, compared to other techniques for quantifying AR, is that it is not affected by the presence of regurgitation of the other heart valves (in contrast to the volumetric MRI). If one adds the simplicity and speed of the single slice technique (in the regular clinical situation, a total time of 20–30 min will be required for preparation, scanning and data analysis) to all advantages above, the conclusion drawn is that it seems the most reliable and convenient noninvasive quantitative approach for AR diagnosis.

On the other hand, all sources of error common in all MRI procedures (blood motion, cardiac motion, respiratory motion, cardiac arrhythmia, and patient motion) could introduce errors in the implementation of this technique and they have to be thoroughly investigated. From the *in vivo* part of this study, it was observed that aortic motion did not affect the reliability of position of the slice between the valve and the coronary ostia, mainly because such a motion does not happen exclusively in the through-slice (through-plane) direction [as seen in this study and based on other reports (30, 31)]. Also, since in diastole cardiac motion is not too rapid (30), a relatively high temporal resolution of the cine PVM acquisition (as in the present study) will take into account, as much as possible, the in-plane motion. Nevertheless, the *in vivo* observations from the present work can only be indicative about the effects of cardiac and respiratory motion. Stronger conclusions about these effects could be drawn from a large amount of clinical data from which more information could be obtained for additional improvement of this approach.

CONCLUSION

In this study, the first important step toward establishing magnetic resonance phase velocity mapping in quantifying aortic regurgitation was taken, by showing that the regurgitant flow rate can be accurately measured by using a single slice between the aortic valve and the coronary ostia level with conventional imaging techniques. Away from the valve, aortic compliance and coronary flow introduce considerable errors in the ARV measurements. The technique is not significantly affected by the presence of acceleration close to the regurgitant orifice. The agreement in the tendency between *in vitro* and *in vivo* results indicates the great potential of the technique clinically.

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