Flow Quantification Using Fast Cine Phase-Contrast MR Imaging, Conventional Cine Phase-Contrast MR Imaging, and Doppler Sonography: In Vitro and In Vivo Validation

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OBJECTIVE. Our purpose was to assess the accuracy of measurements of flow velocity and volume flow rate in an in vitro phantom and in healthy human volunteers using a cardiacgated, segmented K-space, fast cine phase-contrast (PC) MR imaging technique with view sharing (fast PC). We compared this method with conventional cine PC MR imaging and Doppler sonography.

SUBJECTS AND METHODS. Pulsatile flow was generated in a flow phantom that consisted of a cylindric tube having various degrees of tapered stenosis. Phase-encoded velocity maps were obtained using cine PC and fast PC MR imaging. Doppler sonography was also performed. Measurements of aortic and pulmonary artery peak systolic and minimum diastolic velocity and volume flow rate were then compared in eight healthy volunteers using the three imaging techniques.

RESULTS. We found excellent agreement between fast PC and cine PC measurements of peak systolic velocity when regions of interest were drawn to exclude vessel margins (r > .99 for phantom studies, and r = .80 for human studies). Correlation between minimum diastolic velocity measurements by MR imaging was limited by noise that resulted from high encoding velocity settings. However, such correlation improved with signal averaging. When compared with predicted values of volume flow rates, both cine PC (r > .99) and fast PC (r = .97) MR imaging were more accurate than Doppler sonography (r = .78) in vitro. Measurements of cardiac output were adversely affected by low signal to noise, especially during diastole; estimates based on systolic forward flow resulted in better agreement between the two MR imaging methods.

CONCLUSION. Fast PC MR flow quantification may prove to be a useful adjunct to routine MR studies for measurements of peak flow velocity. However, estimates of volume flow rate using fast PC MR imaging are limited because of increased noise during low diastolic flow as well as edge artifacts.

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R cine phase-contrast (PC) flow quantification can provide noninvasive measurements of volume flow rate and flow velocity [1, 2]. Cardiovascular applications have been reviewed [3, 4] and include the quantitative study of flow within the heart across normal and diseased valves; through major cardiothoracic vessels in normal, diseased, and postoperative states; and through systemic vessels including carotid, visceral, and peripheral arteries. In addition, MR PC flow quantification has been advocated as a useful adjunct to MR angiography because it can provide quantitative information about the physiologic effects of anatomic abnormalities, analogous to the role of Doppler sonography in the evaluation of camodified Bernoulli equation and other more sophisticated mathematic derivations to estimate pressure gradients across stenoses based on peak velocity measurements have also been described [8–10].

Several studies have validated cine PC methods of flow quantification in vitro using constant [2, 11–14] and pulsatile [2, 15] flow phantoms. Pelc et al. [16] implanted sonographic blood flow probes in anesthetized dogs to acquire simultaneous sonographic and cine PC MR measurements of volume flow rate. They found a high accuracy of cine PC measurements of pulsatile flow in vivo. In humans, PC and Doppler sonography measurements of flow velocity with in systemic arteries such as the carotid arteries [5] and in cardiac measurements have also been compared [12, 17–21].

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rotid artery disease [5-7]. Application of the

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One major limitation of conventional cine PC methods is the relatively long imaging time that precludes breath-hold imaging, thereby limiting application in the chest and abdomen. Debatin et al. [15] showed that respiratory motion causes blurring of vessel margins and artifactual enlargement of vessel regions of interest, resulting in overestimations of renal artery blood flow both in an in vitro model and in vivo. Shorter imaging times can be used at the expense of decreased temporal resolution. However, for in vivo measurements of pulsatile flow, adequate temporal resolution is essential for accurate determination of peak systolic flow and for assessment of the pattern of velocity waveforms.

With a cardiac-gated, segmented K-space fast PC imaging sequence (fast PC), the acquisition of multiple lines of K-space at several phases of the cardiac cycle during each R-R interval allows high temporal resolution cine PC images to be obtained within a single breathhold [22–26]. Breath-hold fast PC flow quantification has been tested for constant flow and for mildly pulsatile flow in vivo and has been used to quantify coronary artery flow [23]. By sharing views from temporally adjacent data sets, intermediate temporal phases can be generated and scan time can be reduced [25]. Foo et al. [25] have examined the accuracy of a segmented K-space PC technique with view sharing for measuring constant flow rates of 400-1600 ml/min in an in vitro phantom; significant correlation between measurements using this technique, conventional cine PC, and Doppler sonography (using a digital flow meter) were found. Sakuma et al. [26] have applied the technique to show reproducibility of measurements of coronary flow velocity in humans. However, to date, this method has not been validated for pulsatile flow.

Our purpose was to evaluate the accuracy of this cardiac-gated, segmented K-space PC MR imaging method with view sharing, conventional cine PC MR imaging, and Doppler sonography for measurements of flow velocity and volume flow rate through a phantom with various degrees of stenosis. We then compared the three imaging techniques for measurements of pulmonary artery and aortic flow in eight volunteers, with particular attention to factors affecting the implementation of fast PC in a clinical setting.

Subjects and Methods

Flow Phantom

A blood-mimicking fluid (Syn Cut Heavy Duty; Acra Tech, Toronto, Canada) (viscosity, 4.0 cp; T1,

1000 msec; and T2, 100 msec [27]) was used for all flow phantom experiments. The phantom consisted of similar cylindric perspex tubes of 1-cm diameter. each constructed to have a different degree of tapered stenosis 1 cm in length (0%, 50%, 75%). Pulsatile flow was generated at peak flow rates of 10, 20, and 30 ml/sec using a positive displacement pump (University Hospital Development Corporation Flow System; Quest Image, London, Canada) preset to deliver 71 strokes per minute. The phantom was connected to the pump at each end by approximately 2 m of nondistensible reinforced tubing. The pulsatile waveform was programmed to mimic a femoral artery waveform. Constant flow rates were calibrated repeatedly using a stopwatch and graduated cylinder and remained within the manufacturer's estimate of $\pm 1\%$ [27]

Volunteer Subjects

After informed consent was obtained, eight healthy volunteers (six men and two women) who were 26–40 years old underwent MR imaging of the heart and echocardiography, obtained within a 1-month interval. No subjects had a history of heart disease.

MR Studies

All MR studies were obtained using a 1.5-T Signa superconducting system (General Electric Medical Systems, Milwaukee, WI), using 5.4 software and standard gradient hardware.

For phantom studies, the perspex model was positioned centrally within a transmit-receive head coil with ECG gating from the pump's triggering device, preset at 71 beats per minute. Human studies were obtained using a torso phased-array coil [28] and flat ECG leads for cardiac gating.

For both in vivo and in vitro studies, cine PC was obtained using TR/TE = 25/9, flow compensation, and 32 interpolated phases per R-R interval. Imaging time was approximately 2.5 min per acquisition at each anatomic location. Fast PC imaging (Fastcard PC: General Electric Medical Systems [25]) was obtained using TR/TE = 18/9, two views per segment, flow compensation, and view sharing (providing ~20-24 phases per R-R interval). Imaging time was approximately 1 min per acquisition at each anatomic location. Images were processed without magnitude weighting to allow direct quantification from phase images. For both sequences, the following parameters were used: 30° flip angle, 16-cm field of view for phantom studies and 24-26 cm for human studies, 256 × 128 matrix size, 10-mm thickness, and flow sensitivity in one direction only. Velocity encoding was adjusted up to the maximum allowed, 400 cm/ sec. For human studies, a single acquisition was used for all sequences. Signal averaging from various numbers of acquisitions was compared in phantom studies. A 5% trigger window was used for phantom studies: 10% was used for human studies. For all sequences, the bandwidth was ±16 kHz. Technical details of the fast PC pulse sequence have been described [25].

For human volunteers, coronal and axial localizing sequences were used to identify planes perpen-

dicular to the direction of flow for the proximal main pulmonary artery and at the level of the aortic valve. Both were then imaged using a prescribed doubleoblique plane. All human fast PC studies were performed with volunteers instructed to hold their breath at end inspiration.

PC flow quantification measurements are based on the observation that the phase shift of a moving spin in a magnetic field gradient in the direction of flow is proportional to the product of the velocity of the spin and the first moment of the gradient [1]. Images acquired using the phase difference method with PC techniques provide estimates of flow velocity that are represented by pixel intensity values (mm/sec) [4]. The product of the measured velocity (spatially averaged across the region of interest) and the region of interest area provides the volume flow rate (ml/sec). Summing the average flow rate over all frames of the cardiac cycle results in the total forward flow through the vessel per cycle. Regions of interest were manually defined at phantom or vessel margins on the basis of magnitude images and adjusted for each frame. For phantom studies, the region of interest could be verified against the known dimensions of the phantom. Background phase correction was performed using standard software with regions of zero velocity outside the vessel or tube lumen selected manually. All in vitro measurements were obtained at the level of the stenotic portion of the phantoms.

To minimize the effects of noise at the margins of vessels, measurements of maximum velocities were made using regions of interest that were slightly smaller than the lumen of the vessel or tube (0.2–2 cm in diameter).

Sample velocity profiles plotted in this report represent the maximum absolute values measured at each phase of the cardiac cycle so that both peak systolic and minimum diastolic velocity values can be determined from a single profile.

Doppler Sonography

Doppler sonography studies of the flow phantom were obtained using a 7-MHz linear transducer (HDI 3000; Advanced Technology, Bothell, WA) to measure peak velocity, end diastolic velocity, and average flow volume rates using the Hi-Q software package. For volume flow rate measurements, the sampling volume was adjusted to include the entire diameter of the lumen examined. The Doppler angle was kept below 60° for all studies using a standoff pad. The overall distance between transducer and phantom was kept less than 2 cm. For volume flow rate estimates, the sample volume extended across the entire lumen diameter. All in vitro measurements were made at the level of the stenotic portion of the phantoms.

All volunteers underwent echocardiography using a 2.5-MHz transducer (HP Sonos 2500; Hewlett-Packard, Palo Alto, CA). Valvular flow was evaluated by pulsed and continuous wave Doppler in the four-chamber long-axis view. Pulsed Doppler measurements of velocity were used for comparisons with MR measurements.

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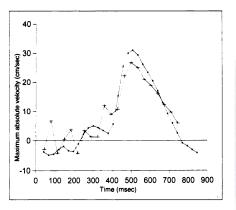


Fig. 1.—Representative velocity profiles obtained with nonstenotic phantom with pulsatile flow at peak flow rate of 20 ml/sec. Flow velocities were measured by cine phase-contrast (PC) (TR/TE, 25/9) () and fast PC (18/9) (+) MR imaging. MR measurements were made by positioning region of interest centrally within lumen of tube (without including edges, when possible) and recording maximum absolute values at level of stenosis; peak systolic and minimum diastolic values can be estimated from each waveform. Encoding velocity was 200 cm/sec. At lower velocities, fast PC MR measurements consistently had lower signal to noise than cine PC MR measurements.

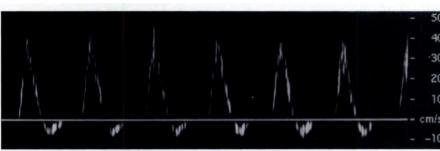


Fig. 2.—Doppler sonography velocity profile obtained with nonstenotic phantom at peak flow rate of 20 ml/sec. All Doppler measurements were performed with sample volume equal to diameter of tube.

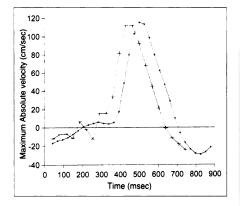


Fig. 3.—Velocity profiles obtained with phantom with 50% stenosis at peak flow rate of 20 ml/sec. Measurements were made by cine phase-contrast (PC) (■) and fast PC (+) MR imaging with encoding velocity of 200 cm/sec.

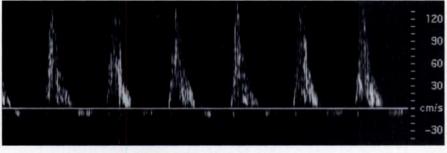


Fig. 4.—Doppler sonography velocity profile obtained with phantom with 50% stenosis at peak flow rate of 20 ml/sec.

Statistical Analysis

Comparisons among measurements using the two MR imaging techniques and Doppler sonography were made on the basis of correlation coefficients, linear regression, and analysis of variance using Excel (Microsoft, Redmond, WA).

Results

Phantom Studies

Representative velocity waveforms, obtained using cine PC, fast PC, and Doppler

sonography for tubes with 0%, 50%, and 75% stenoses subjected to pulsatile flow at a maximum flow rate of 20 ml/sec, are shown in Figures 1–6.

Agreement among the three methods was evaluated on the basis of measurements of peak systolic velocity and minimum diastolic velocity across a range of stenoses and flow rates (Figs. 7–9). Results of linear regression analyses are also shown in Figures 7–9. For peak velocities, the relation between fast PC and cine PC measurements approached the line of iden-

tity (Fig. 7; fast PC peak velocity = 1.00x - 1.63 cm/sec, where x represents peak systolic velocity determined using cine PC; r > .99; standard error of the estimate [SEE] = 6.27 cm/sec). Similar agreement was found for peak velocities between fast PC and Doppler sonography (Fig. 8; SEE = 5.34 cm/sec) and for cine PC and Doppler sonography (Fig. 9; SEE = 4.57 cm/sec). Using two-way analysis of variance, no statistically significant difference in measurements of peak systolic velocity was found among the three methods.

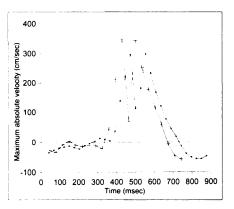


Fig. 5.—Velocity profiles obtained with phantom with 75% stenosis at peak flow rate of 20 ml/sec. Measurements were made by cine phase-contrast (PC) (■) and fast PC (+) MR imaging with encoding velocity of 400 cm/sec, maximum allowable with our software. Predictable aliasing artifact was observed with both MR imaging methods.

For measurements of minimum diastolic velocity, fast PC velocity plots consistently showed more noise (and lower signal to noise) than cine PC velocity plots (Fig. 1), as reflected by lower correlation coefficients (r = .93 between fast PC and cine PC and r = .74 between fast PC and Doppler sonography). Repeat measurements using averages of two and four acquisitions improved correlation for measurements of minimum diastolic velocity.

The total volume flow rate could be predicted by knowing volumes displaced by the piston per stroke, assuming nondistensible tubing. On the basis of predicted values, cine PC provided more accurate measurements of volume flow rate than fast PC, especially at lower velocities (Table 1). Both fast PC (r = .97) and

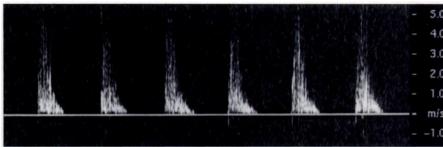


Fig. 6.—Doppler sonography velocity profile obtained with phantom with 75% stenosis at peak flow rate of 20 ml/sec.

cine PC (r > .99) measurements of volume flow rates correlated better with predicted values than did Doppler sonography (r = .78). Doppler measurements of volume flow were based on time-averaged mean velocities measured across the entire lumen (sample volume diameters ranged from 0.25 to 1 cm, depending on the phantom used) multiplied by cross-sectional area.

Human Studies

Initial attempts to measure peak systolic and minimum diastolic velocities in the aorta and pulmonary arteries of healthy volunteers used regions of interest manually drawn around the lumen-vessel wall interface defined on the basis of the magnitude images. However, inclu-

sion of the vessel boundary led to wide fluctuations in the maximum velocity measurements across the cardiac cycle, particularly during diastole. Therefore, for measurements of maximum flow velocity, smaller regions of interest were centered within the lumen; regions of interest of 1 cm in diameter provided consistent values for peak systolic velocity across data sets.

Peak systolic velocity measurements in humans using cine PC and fast PC were compared by means of linear regression (Figs. 10–13). The following equation describes the best-fit line for both aortic and pulmonary artery peak systolic flow data: fast PC peak velocity = 1.05x - 0.63 cm/sec (where x = peak systolic velocity measured using cine PC), r = .80, and SEE = 10.94 cm/sec (Fig. 10). Lower agreement was

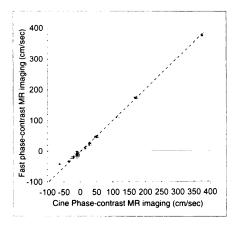


Fig. 7.—Graph shows correlation between measurements of peak systolic and minimum diastolic velocity for all types of phantoms using fast phase-contrast (PC and cine PC MR imaging. Best line of fit (y = 1.00x - 1.63) is shown (dashed line); $r > .99. \square = 0\%$ stenosis, $\Delta = 50\%$ stenosis, * = 75% stenosis.

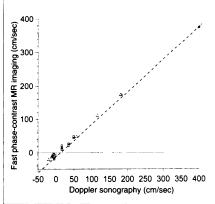


Fig. 8.—Graph shows correlation between measurements of peak systolic and minimum diastolic velocity in vitro using fast phase-contrast MR imaging and Doppler sonography. Best line of fit (y = .96x - 3.98) is shown (dashed line); r > .99. $\square = 0\%$ stenosis, $\Delta = 50\%$ stenosis, x = 75% stenosis.

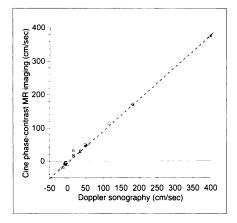


Fig. 9.—Graph shows correlation between measurements of peak systolic and minimum diastolic velocity in vitro using cine phase-contrast MR imaging and Doppler sonography. Best line of fit (y = 0.94x - 0.56) is shown (dashed line); r > .99. $\square = 0\%$ stenosis, $\Delta = 50\%$ stenosis, * = 75% stenosis.

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found for peak systolic velocity measurements using fast PC and Doppler echocardiography (Fig. 11; r = .79, SEE = 11.91 cm/sec) and for measurements using cine PC and Doppler echocardiography (Fig. 12; r = .69, SEE = 10.06 cm/sec).

Flow volume measurements using cine PC and fast PC were based on measurements of spatially averaged velocities multiplied by crosssectional area of vessel lumen for each phase of the cardiac cycle. Initially, measurements of cardiac output were computed on the basis of the sum of flow measurements for all phases of the cardiac cycle. The correlation between cine PC and fast PC measurements of total volume of flow was low (r = .17, SEE = 1141 ml), with fast PC estimates consistently exceeding cine PC estimates. However, because greater noise was observed at low flow rates during diastole for both in vitro and in vivo measurements (Fig. 1), a second estimate of cardiac output was made using only flow during systole (measured to the point of reversal of flow, typically about 400 msec). The correlation coefficient calculated using this method was .74, and the best-fit line approached the line of identity (fast PC cardiac output = 1.07x - 219.7 ml, where x = cardiac output measured using cine PC; SEE = 632 ml).

Flow volume measurements using Doppler sonography in vivo were not estimated because of limitations in estimating average velocities across the luminal areas and in measuring valvular cross-sectional area across all phases of the cardiac cycle.

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Fig. 10.—Graph shows correlation between measurements of peak systolic flow velocity in aorta (x) and pulmonary artery (+) of eight healthy volunteers using fast phase-contrast (PC) and cine PC MR imaging. Best line of fit (y = 1.05x - 0.63) is shown (dashed line); r = .80.

TABLE I	In Vitro Volume Flow Measurements Using Phase-Contrast (PC), Cine PC and Doppler Sonography						
Stenosis ^a (%)	Peak Rate	In Vitro Volume Flow Measurements (ml/min)					
	(ml/sec)	Fast PCb	Cine PC ^b	Sonography ^b	Predicted ^c		
0	10	103.2 ± 67.4	97.0 ± 21.2	124.5 ± 9.0	82.2		
	20	206.4 ± 35.3	167.7 ± 0.9	275.5 ± 16.5	164.3		
	30	358.2 ± 24.5	265.7 ± 8.0	344.6 ± 69.1	246.5		
50	10	95.8 ± 4.0	85.8 ± 1.8	88.3 ± 5.9	82.2		
	20	174.0 ± 8.0	171.0 ± 8.3	150.3 ± 8.8	164.3		
	30	301.5 ± 40.5	278.0 ± 42.6	207.2 ± 0.0	246.5		

^aData from measurements using the 75% stenosis phantom are not included because of artifacts introduced by aliasing despite a maximum encoding velocity of 400 cm/sec.

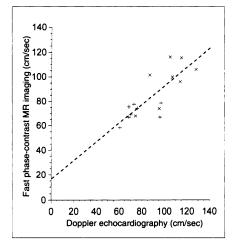
bMeasurements are given as average ± SD.

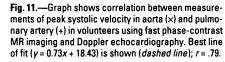
Discussion

Our in vitro studies using nonstenotic and stenotic phantoms found comparable measurements of peak systolic velocity by conventional and fast cardiac-gated cine PC. Velocities attained using a pulsatile pump system ranged from 0 to 400 cm/sec, representative of the range of physiologic and pathologic flow velocities. The in vitro system also allowed comparison of the two MR techniques with Doppler sonography in a setting free of several variables that can limit in vivo comparisons and applications. Specifically, partial volume effects were minimized because geometry and dimensions of the phantom were known a priori. Vessel motion artifacts causing apparent increases in cross-sectional area [4, 15] were also eliminated. However, edge spike artifacts, resulting

from signal loss near vessel edges [29], were still observed in vitro, particularly for fast PC images. Meaningful measurements of peak systolic flow could be obtained only when regions of interest were defined to exclude the vessel edges. In this setting, the agreement among the three techniques for measuring peak velocity was high (r > .99 for all combinations).

Measurements of minimum diastolic velocity showed lower agreement. As described by Pelc et al. [4], the SD for measurements of velocity, σ_v , is linearly dependent on the encoding velocity (Venc) and inversely proportional to the signal-to-noise ratio (SNR). The Venc values were selected on the basis of expected peak systolic velocity measurements; thus the SD of measurements of minimum diastolic velocity values was predictably high [30, 31]. Further-





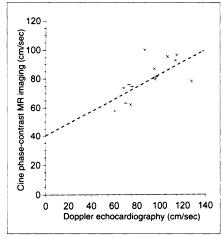


Fig. 12.—Graph shows correlation between measurements of peak systolic velocity in aorta (x) and pulmonary artery (+) in volunteers using cine phase-contrast MR imaging and Doppler echocardiography. Best line of fit (y = 0.44x + 39.97) is shown (dashed line); r = .69.

^cPredicted values are based on known volumes of displacement by piston pump and peak volume flow rates programmed for selected pulsatile waveform

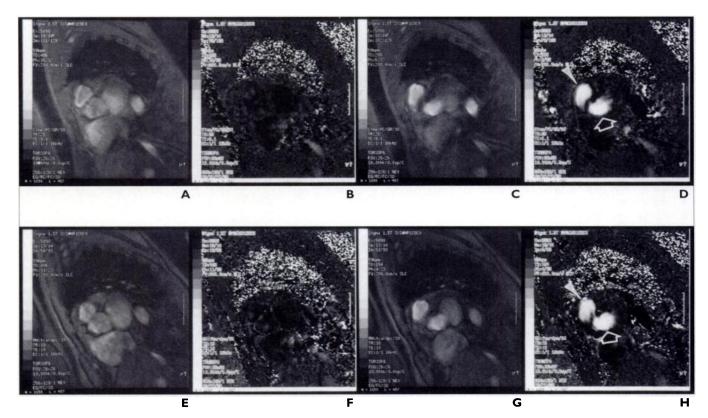


Fig. 13.—Double oblique-phase images obtained in plane of aortic valve and pulmonary artery in healthy human volunteer during diastole (A, B, E, and F) and at peak systole (C, D, G, and H) with cine phase-contrast (PC) (TR/TE, 25/9; A–D) and fast PC (18/9; E–H) MR techniques. Phase-encoding was performed perpendicular to imaging plane, and encoding velocity was set at 200 cm/sec. Magnitude images (A, C, E, and G) also provide anatomic landmarks. Increased flow during systole across aortic valve (arrows, D and H) and pulmonary artery (arrowheads, D and H) is reflected on phase-encoded images by increased signal intensity. Measurements of velocities were made by directly placing regions of interest within lumen of vessels on phase images.

more, fast PC inherently has a lower SNR compared with cine PC (decreased acquisition time with fast PC), which may explain the lower agreement between fast PC and Doppler sonography or cine PC at lower velocities and the increased noise seen on individual plots of velocity (Fig. 1). Increasing SNR by increasing the number of acquisitions improved correlation by reducing σ_v . The increased noise at lower flow rates may also explain in part the slightly lower accuracy of volume flow rate measurements using fast PC than using cine PC when compared with predicted values.

Measurements of peak velocity in the aorta and pulmonary artery in eight healthy volunteers showed good agreement. The greater discrepancy between measurements of peak velocity using cine PC and fast PC in vivo may be due to the effects of beat-to-beat variations, partial volume effects (selection of regions of interest), higher order motion, and motion blurring. Moreover, the cine PC MR measurements were obtained during quiet respiration, whereas fast PC MR measurements were made during breath-hold, and physiologic differences may have also contributed to discrepancies in measurements. The compari-

son between Doppler echocardiography and MR imaging is further limited by the effect of examining volunteers on different days.

Although lower SNR and high Venc settings limited the accuracy of fast PC measurements of flow velocity during diastole, the lower SNR may have been compensated for in part by decreased motion blurring during fast PC acquisitions. We found greater agreement between fast PC and Doppler measurements of peak flow than between the non-breath-hold cine PC and Doppler measurements. Where accurate diastolic velocity measurements are desired, repeating the sequence with lower V_{enc} may be necessary. Alternatively, phase unwrapping [32] and variable V_{enc} [33, 34] techniques may improve the dynamic range of PC measurements of flow. Buonocore and Bogren [30] and Ståhlberg et al. [31] have also shown that the effects of higher order flow causing spin dephasing (and breakdown of the linear phase-velocity relationship) can be minimized by using lower echo times.

Using a pulsatile flow phantom, absolute flow volumes can be predicted on the basis of the known volume of fluid displaced by the piston per cycle. Doppler sonography proved significantly less accurate for measuring volume flow rate than either MR technique. Doppler estimates rely on accurate determinations of average velocity across the entire intraluminal flow profile. Despite the use of optimal imaging parameters [35], our results do not support the routine use of Doppler sonography for measurements of flow volume rate and are consistent with previous findings [36, 37]. New Doppler techniques for estimating volume flow remain to be verified.

We observed that fast PC is less accurate than cine PC in determinations of flow volume rate, particularly at lower velocities. This finding most likely is a result of the decreased SNR of fast PC at low diastolic velocities. Edge spike artifacts also diminish the accuracy of both techniques. Both methods would likely be improved by implementing automated region-of-interest techniques [38] and algorithms that are less sensitive to partial volume effects such as complex difference techniques [39]. Although improved correlation between the two methods could be attained using systolic forward flow measurements only, this modification restricts clinical application because the contribution of diastolic flow is unknown.

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Modifications such as a variable V_{enc} may improve the method [33, 34].

The cardiac-gated, segmented K-space cine PC technique with view sharing places MR flow quantification in the realm of breath-hold techniques. With a TE of 9 msec, our 1-min sequence allowed more than 20 frames per R-R interval. With lower TEs now possible, sequences can be obtained more comfortably within the time frame of a breath-hold while maintaining high temporal resolution. This fast MR imaging approach has the advantages of wide availability and ease of implementation with conventional gradient systems. As a quick breath-hold technique that can be obtained as an adjunct to MR angiography, fast PC can provide accurate estimates of peak systolic flow that may supplant Doppler sonography in the evaluation of the hemodynamic significance of atherosclerotic disease. However, in their present forms, neither fast PC imaging nor Doppler sonography provides sufficiently accurate measurements of volume flow rates to justify clinical use.

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