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ORIGINAL ARTICLE

Spatial factors for quantifying constant flow velocity in a small tube phantom: comparison of phase-contrast cine-magnetic resonance imaging and the intraluminal Doppler guidewire method

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Abstract
Purpose. We examined the spatial factors influencing magnetic resonance (MR) flow velocity measurements in a small tube phantom and used the same measurements obtained with an intraluminal Doppler guidewire as reference.
Materials and methods. We generated constant flow velocities from approximately 40 to 370 cm/s in a tube 4 mm in diameter. We then performed segmented k-space, phase-contrast cine-MR imaging to quantify spatial peak flow velocities of one pixel and of five adjacent pixels as well as spatial mean velocities within regions of interest in a cross section of the phantom. Pixel dimensions ranged from 1.00 × 1.00 mm to 2.50 × 2.50 mm. We compared the MR measurements with the temporally averaged Doppler spectral peak velocities.
Results. For one pixel ($r > 0.99$: MR flow velocity for pixel dimension 1.00 × 1.00 mm = 1.03x + 9.8 cm/s), the linear correlation was excellent between flow velocities by MR and Doppler guidewire methods. However, for the five adjacent pixels, MR measurements were significantly underestimated using pixels 1.25 × 1.25 mm to 2.50 × 2.50 mm and for mean velocities for all pixel dimensions.
Conclusion. Relatively high spatial resolution allows accurate MR measurement of constant flow velocity in a small tube at spatial peak velocities for one pixel.

Key words Flow velocity quantification · Intracoronary Doppler guidewire · Phantom experiment · Phase-contrast cine-magnetic resonance imaging

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Introduction

Magnetic resonance imaging (MRI) quantification seems a reasonable alternative to the intraluminal Doppler guidewire method, clinically the most accurate technique, for coronary flow velocity measurement because MRI is noninvasive and requires neither radiation nor nephrotoxic contrast medium. However, it is difficult because coronary arteries are small and subject to both cardiac and respiratory motion. A cardiac-gated, segmented k-space, phase-contrast (PC) cine technique allows data acquisition within a single breath-hold to provide a phasic flow-velocity time curve for coronary arteries in the cardiac cycle. This method has been commonly used to determine temporal peak coronary flow velocity and coronary flow velocity reserve.[1–3] Nevertheless, absolute and reserve flow velocities measured by both the Doppler guidewire method and MRI can disagree because temporal and spatial factors affect MRI measurements. The use of view-sharing reconstruction, better receiver coils, and stronger gradient systems can improve temporal resolution;[4] and improved navigator-guided, free-breathing methods can

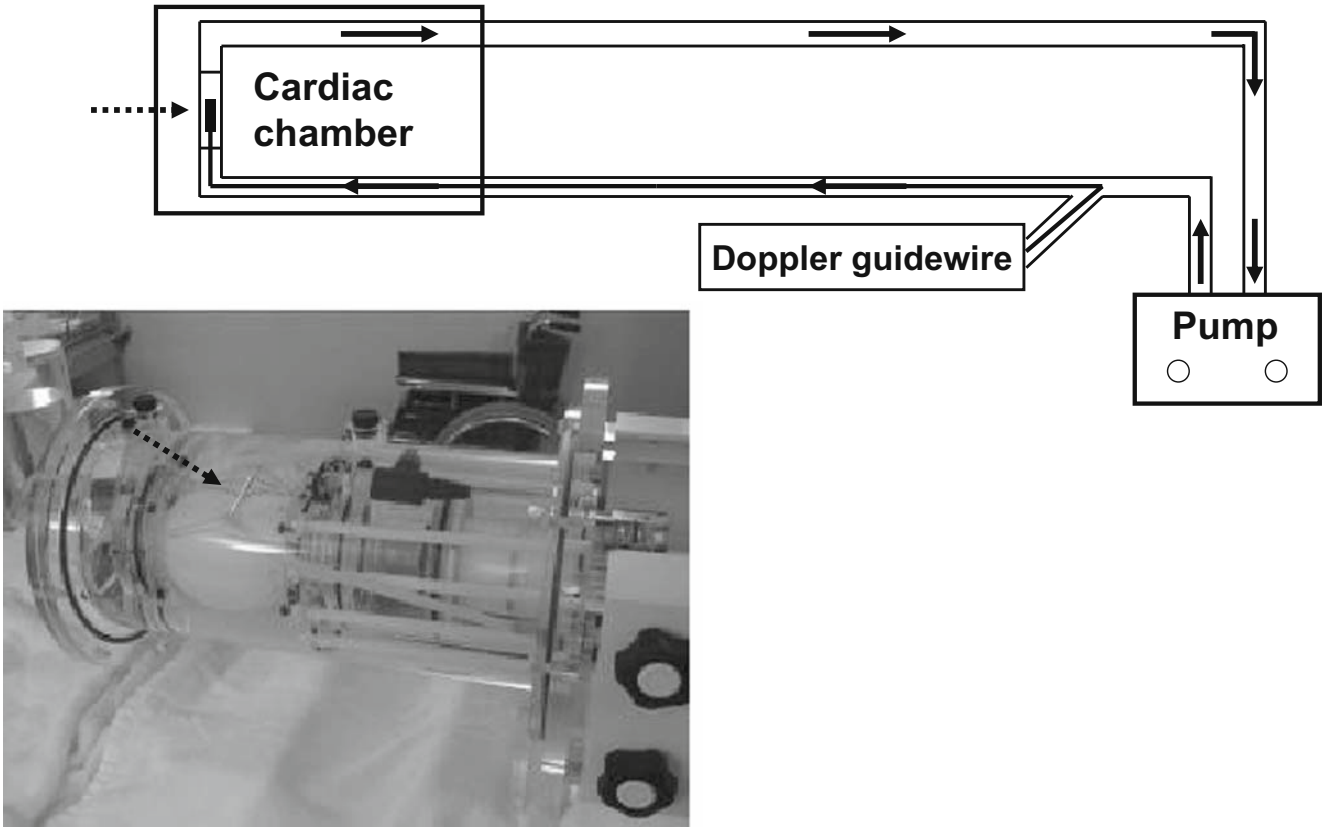

Fig. 1. Overview of the original flow phantom. A straight cylindrical acryl tube 4 mm in inner diameter and 5 cm long (*dotted arrows*) on a plastic chamber (*Cardiac chamber*) was connected at each end by nondistensible hose to the original computer-controlled flow pump (*Pump*) placed outside the examination room. In this circuit, we circulated blood-mimicking fluid in the flow direction (*solid arrows*). A Doppler guidewire was introduced into the phantom via a side port of the proximal hose. This study was performed without pulsating the cardiac chamber

reduce respiratory artifacts.[5] However, spatial factors affecting accurate measurement using PC cine-MRI have not been thoroughly investigated.

Therefore, we used segmented k-space, PC cine-MRI to measure absolute constant flow velocity in a small tube phantom simulating stationary coronary arteries and compared the MRI and Doppler guidewire measurements. We did not expect temporal factors to affect experimental results significantly, and we could determine spatial factors somewhat arbitrarily in this situation. We then investigated the impact of systematic spatial factors—including in-plane spatial resolution and mean versus peak spatial flow velocity within the region of interest (ROI)—on MRI measurement accuracy.

Methods and materials

Flow phantom

We constructed an original flow phantom (Fig. 1) from a straight cylindrical acryl tube (4 mm inner diameter, 5 cm long) connected at each end by nondistensible hose to an original computer-controlled flow pump (Alpha Flow SV Pro1; Fuyo, Tokyo, Japan). The tube's inner diameter was within the expected range of mean normal proximal coronary artery diameters measured by MRI (4.1 ± 0.8 mm) or conventional coronary angiography (3.9 ± 0.6 mm).[6,7] We submerged the phantom in degassed water filling a plastic chamber placed on the MRI scanner bed in front of the gantry, and we placed the pump outside the examination room to avoid difficulties from the magnetic field.

In this circuit, we circulated blood-mimicking fluid for Doppler ultrasonography (US) (test fluid 707; ATS Laboratories, Bridgeport, CT, USA) with a fluid density of 1.04 g/cm^3 and viscosity 1.69 g/cm·s; it consisted of glycerin, degassed water, and 30 μm of polystyrene microspheres. The pump generated a constant flow at various velocities within the phantom and directed parallel to the magnet bore. All measurements utilized an electrocardiographic (ECG) pattern simulated by the pump's computer of a heart rate of 60 beats per minute. We confirmed the constancy of the computer's meter for

flow volume during each flow velocity measurement by both Doppler guidewire imaging and MRI.

Intracoronary Doppler guidewire

We predetermined constant flow velocities from approximately 40 to 370 cm/s, averaging the time of instantaneous spectral peak velocity (APV), measured by a 0.014-inch, 175-cm long, flexible, steerable intracoronary Doppler guidewire with a 12-MHz piezoelectric US transducer integrated onto its tip (FloWire System; Volcano, Rancho Cordova, CA, USA). The transducer was located 4.2–5.2 mm distal to the tip of the guidewire and had a sample volume of 4 mm diameter and 1 mm depth, with an aperture of 45°. A fast online Fourier frequency analysis (more than 100 spectra/s) provided the basis for continuous tracking of the upper edge of the frequency spectrum, which corresponded to the instantaneous peak velocity. APV was automatically computed based on segments consisting of the envelope of the phasic velocity spectrum during two cardiac cycles. Specifically, on each flow velocity measurement, the guidewire was introduced into the phantom via a side port of the proximal hose and connected to the real-time, gray-scale spectral analyzer (FloMap System; Volcano) outside the room. We rotated the guidewire to optimize the audio signal. APV and flow spectrum were instantaneously displayed on the spectral analyzer and were confirmed constant when minimum or no fluctuation was apparent for 1 min.

After confirming constancy, we recorded Doppler measurements of the APV and flow spectrum for later review on a computer connected online to the spectral analyzer, with ECG gating from the pump's triggering signal for 3 min. We left the guidewire in place in the phantom during subsequent MRI measurements of the same flow velocity under the same flow conditions.

Finally, following each MRI quantification, we confirmed the constancy of the APV and flow spectrum displayed on the spectral analyzer during 1 min and compared them with those obtained before each MRI measurement. We repeated these procedures for different velocities. We averaged the APV measurements for 3 min and used the averages as the Doppler guidewire flow velocities ($V_{Doppler}$) and compared them with the MRI measurements.

We used the Reynolds number utilized to calculate the degree of flow turbulence for the different velocities:

$$\text{Reynolds number} = \rho V d/\mu$$

where ρ (g/cm^3) is the fluid density; V (cm/s) is the flow velocity; d (cm) is the diameter of the tube; and μ (g/cm·s) is the viscosity.

Phase-contrast cine-MRI

We obtained all MRI data with a 1.5-tesla superconducting system (Magnetom Avanto; Siemens Medical Systems, Erlangen, Germany). We moved the phantom on the scanner bed into the gantry horizontally at a constant height and positioned it centrally between the transmit–receive, eight-channel phased-array pelvic coil covering the anterior aspect of the chamber and the spine coil covering the posterior aspect. We used ECG gating from the pump's triggering signal.

Localizer images were used to select a plane perpendicular to the phantom's flow direction and acquired retrospective ECG-gated, segmented k-space, PC cine-MRI scans of the cross section of the phantom lumen as close as possible to the indwelling guidewire tip to avoid susceptibility artifact by the guidewire. Specifications were as follows: field of view (FOV) 32 × 32 cm; section thickness 6 mm; repetition time (TR)/echo time (TE) 50/5.6 ms; flip angle 15°; three segments; bandwidth 710 Hz/pixel; 20 frames per R-R interval). After quantification by the Doppler guidewire method, we measured each flow velocity in the phantom using reconstructed magnitude and phase images for five in-plane pixel dimensions—1.00 × 1.00 mm; 1.25 × 1.25 mm; 1.67 × 1.67 mm; 2.50 × 2.50 mm; 2.40 × 1.67 mm—with generalized autocalibrating partially parallel acquisition (GRAPPA), reduction factor 2. The last one was regarded as a more clinically available sequence, in which patients can generally tolerate one breath-hold (Table 1). Velocity-encoding gradients were applied along only the section-selection direction that coincided with the flow direction. To avoid aliasing, velocity encoding (VENC) was determined at a level 30%–50% higher than each APV measured by the Doppler guidewire method.

Aided by a magnitude image, we manually placed circular ROIs within the cross section of the phantom lumen, ensuring that they enclosed the entire lumen (Fig. 2). We measured the spatial peak and average velocities

Table 1. Magnetic resonance imaging profiles by in-plane pixel dimensions

In-plane pixel dimensions (mm)	Matrix	Average	PAT mode	Scan time
1.00 × 1.00	320 × 320	3	None	6′ 55″
1.25 × 1.25	256 × 256	3	None	4′ 22″
1.67 × 1.67	192 × 192	3	None	3′ 14″
2.50 × 2.50	128 × 128	3	None	2′ 11″
2.40 × 1.67	134 × 192	1	GRAPPA 2	25″

PAT, parallel acquisition technique; GRAPPA 2, generalized autocalibrating partially parallel acquisition, reduction factor 2

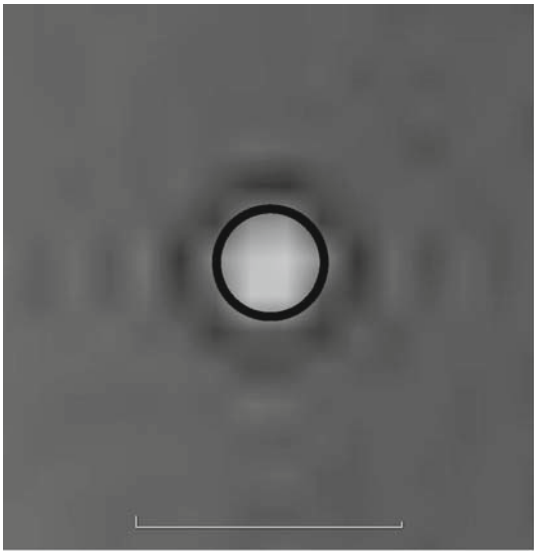

Fig. 2. Phase-contrast cine-magnetic resonance imaging (MRI) of the cross section of the tube lumen. Aided by a magnitude image without artifacts, we manually placed a circular region of interest (ROI) within the cross section of the tube lumen, ensuring that it enclosed the entire lumen

in the ROI on the corresponding phase image and repeated both measurements for all phases using the same ROI for each frame to depict the phasic time–velocity curves of the entire ECG-gated R-R interval. Then, we carefully checked the phase images and the phasic time–velocity curves for aliasing and measurement fluctuation and confirmed the adequacy of each measurement.

We analyzed data using commercial software (ARGUS; Siemens Medical Systems). We defined the spatial peak velocity of one pixel (V_{max1}) as its maximal velocity and that of five pixels (V_{max5}) as the averaged maximal velocity measurements of a central pixel and the four surrounding pixels within the ROIs placed as above. In addition, the spatial mean velocities (V_{mean}) were defined as the average velocity measurements of all pixels within the ROIs.

Thereafter, we moved the phantom on the scanner bed horizontally from the gantry and repositioned it at the same site for Doppler measurements, and we adjusted the pump to obtain different flow velocities for the following measurement. Thus, we repeated further measurements by Doppler guidewire imaging and PC cine-MRI.

Statistical analysis

We compared measurements of flow velocity by MRI (V_{max1}, V_{max5}, V_{mean}) and the Doppler guidewire method ($V_{Doppler}$) using a two-variable linear regression analysis and tested the correlation coefficient for significant differences. We also employed the Bland and Altman analysis to determine the 95% limits of agreement, equivalent to ±2 standard deviations (SD).[8] We determined the mean proportional difference for this analysis using the absolute difference of both measurements divided by the average of both measurements and assessed the significant difference from zero using Wilcoxon's signed-ranks test. $P < 0.05$ was regarded as statistically significant.

Results

The Reynolds number for all velocities did not exceed 2500, considered the critical number in this experiment.

We found statistically significant excellent linear correlations ($r \geq 0.98$) between PC cine-MRI and Doppler guidewire measurements of constant flow velocity; all P values were <0.05 (Fig. 3). MRI measurements of flow velocity likely decreased sequentially as spatial resolution declined and at the same spatial resolutions—in order as V_{max1}, V_{max5}, and V_{mean}. V_{max1} allowed accurate MRI measurements of constant flow velocity with pixel dimension of 1.67 × 1.67 mm (MRI flow velocity = 0.99x − 0.9 cm/s). V_{max1} in pixels of 1.00 × 1.00 mm (P = 0.008) and 1.25 × 1.25 mm (P = 0.038) was significantly overestimated and less accurate than that in pixels of 1.67 × 1.67 mm. Although higher spatial resolution produced more accurate MR measurements using V_{max5} and V_{mean}, there were systemic underestimations of MRI flow velocity measurements relative to Doppler guidewire measurements using V_{max5} with pixel dimensions of 1.25 × 1.25, 1.67 × 1.67, 2.50 × 2.50, and 2.40 × 1.67 mm and using V_{mean} with all pixel dimensions (all P values were <0.05), according to the Bland and Altman analysis and the proportional differences of the flow velocity measurements by both modalities (Table 2).

Discussion

Although PC cine-MRI has been sufficiently validated and clinically applied for coronary flow quantification,[1,9–11] the relation between this accurate measurement and MR spatial factors has not yet been fully investigated. Thus, we compared the constant flow velocity measurement in a small tube phantom using segmented k-space, PC cine-MRI with that obtained by the intraluminal Doppler guidewire method as a reference modality and estimated the impact of systemic spatial factors on the accuracy of the MRI quantification. We found excellent linear correlations between both

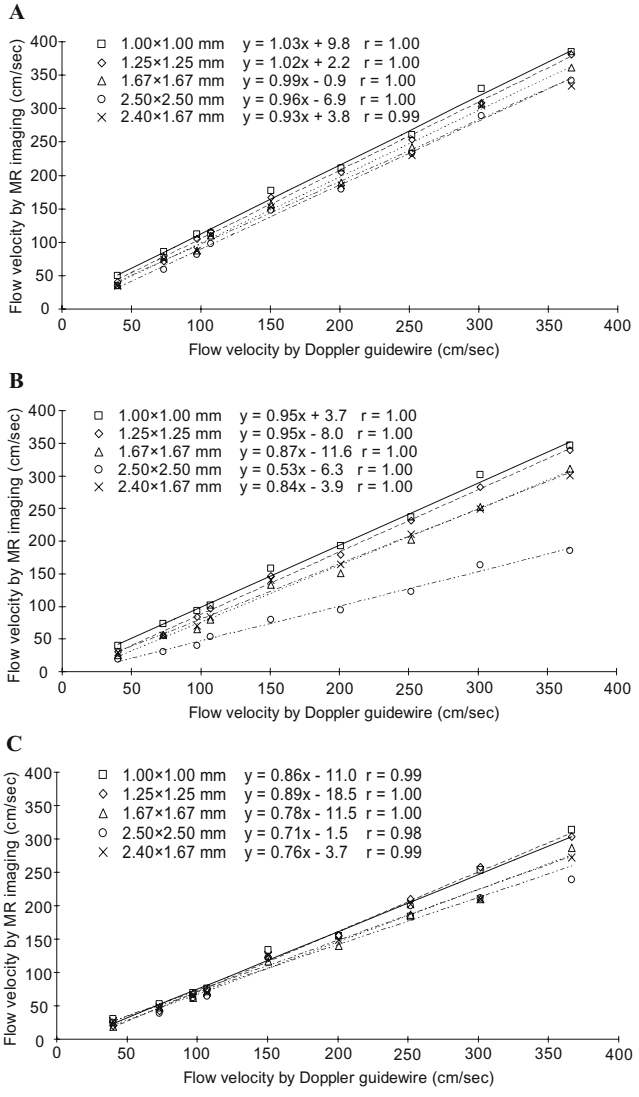

Fig. 3. Linear regression analysis of in vitro constant flow velocity measurements by intraluminal Doppler guidewire imaging (x axis) and phase-contrast cine-MRI (y axis). The data markers represent the flow velocity measurements using the spatial peak velocities of a single pixel (**A**) and of five pixels (**B**) and the spatial mean velocities (**C**) within the ROIs on pixel dimensions of 1.00 × 1.00, 1.25 × 1.25, 1.67 × 1.67, 2.50 × 2.50, and 2.40 × 1.67 mm. The regression lines, equation, and correlation coefficients are shown

measurements; relatively high spatial resolution allowed accurate MRI measurements of constant flow velocity using V_{max1}. In contrast, MR measurements of constant flow velocity using V_{max5} in lower spatial resolutions and V_{mean} were less accurate and revealed systemic underestimations.

For constant flow, laminar flow usually becomes turbulent when the Reynolds number exceeds 2500. Meier and colleagues showed incorrect MR flow quantification using PC techniques, presumably because turbulent flow resulted when the Reynolds number exceeded approximately 3000 in phantom experiments.[12] Because the Reynolds number we calculated was confirmed to be below the critical number, the flow was considered laminar; thus, errors caused by turbulent flow can be ignored in the present study.

Laminar flow velocity usually encountered in clinical settings is highest at the vessel's center and lowest at the vessel's margin in a parabolic manner. Most clinical studies using PC cine-MRI for velocity measurements have provided the spatial mean velocity within the ROI, but Doppler guidewire imaging generally detects the spatial peak velocity in the laminar flow. This methodological difference caused measurements of flow velocity by MRI to be underestimated compared with those obtained by Doppler guidewire imaging, presumably because of intervoxel averaging.[5,13–16]

The commercial software we used can show the spatial peak velocity measurements of a single pixel and five adjacent pixels as well as the spatial mean velocity measurements within the ROIs by MRI. Methodologically, V_{max1} is more similar to $V_{Doppler}$ than V_{max5} and V_{mean} within the same spatial resolutions. Thus, we hypothesized the usefulness of V_{max1} for accurate flow velocity quantification and compared V_{max1}, V_{max5}, and V_{mean} with $V_{Doppler}$. To our knowledge, this approach had not been investigated. Our experimental results suggest that V_{max5} and V_{mean} tend to be more accurate at higher spatial resolution but that V_{max5} at lower spatial resolutions and V_{mean} are significantly underestimated because these sampling pixels, which are much larger than the sample volume of the Doppler guidewire method, can include pixels of lower velocities nearer the vessel boundary and stationary tissue such as the vessel wall and surrounding tissue. In contrast, the spatial peak velocity of a single pixel allows accurate MRI measurements at relatively high spatial resolutions. However, V_{max1} can still be underestimated because it is almost impossible to place the pixel displaying the velocity measurement exactly in the center of the cross section of the lumen on MRI.

In laminar flow, different velocities are found even within a single pixel, and an average value rather than the maximum flow velocity is measured, which induces an error of approximately 2.5% as intravoxel phase dispersion.[9] This suggests that lower velocities nearer the vessel boundary are included even in the single pixel for MRI measurement of flow velocity, which leads to an underestimation of this measurement. The current in-plane pixel dimension of MRI imaging (approximately 1 mm^2) may not be sufficient to quantify coronary flow velocity accurately;[9,17] this underestimation can be reduced only by improved spatial resolution.[5] Consequently, MRI measurements using V_{max1} increased

Table 2. Proportional differences of in vitro constant flow velocity measurements between phase-contrast cine-MRI and Doppler guidewire imaging

	In-plane pixel dimensions (mm)				
MRI measurements	1.00 × 1.00	1.25 × 1.25	1.67 × 1.67	2.50 × 2.50	2.40 × 1.67
V_{max1} [a]	11.4 ± 15.5[d]	3.6 ± 8.9[d]	−1.9 ± 12.5	−10.0 ± 11.6[e]	−4.6 ± 12.9
V_{max5} [b]	2.1 ± 7.5	−12.1 ± 15.4[e]	−22.9 ± 16.7[e]	−52.1 ± 9.2[e]	−19.9 ± 13.2[e]
V_{mean} [c]	−22.7 ± 13.9[d]	−26.9 ± 24.3[e]	−31.8 ± 18.6[e]	−32.0 ± 19.0[e]	−28.2 ± 13.3[e]

Values are expressed as mean proportional difference ± 95% limit of agreement (2 SD) (proportional difference in % = absolute difference of the two measurements/average of the two measurements)
MRI, magnetic resonance imaging
[a] Spatial peak velocity of one pixel
[b] Spatial peak velocity of five pixels
[c] Spatial mean velocity
[d] MRI measurements are significantly underestimated compared with the Doppler imaging measurements ($P < 0.05$)
[e] MRI measurements are significantly overestimated compared with the Doppler imaging measurements ($P < 0.05$)

according to improved spatial resolution in our study. V_{max1} in pixels of 1.00 × 1.00 and 1.25 × 1.25 mm was significantly overestimated and less accurate than that in pixels of 1.67 × 1.67 mm, although we had hypothesized that V_{max1} in the highest spatial resolution allowed the most accurate MRI measurement. The accuracy of flow velocity quantification by Doppler guidewire imaging may need to be estimated.

Phase-contrast cine-MR imaging combined with parallel imaging, such as sensitivity-encoding (SENSE), was effectively applied to quantify flow volume and shunt in pediatric congenital heart disease by substantively reducing the scanning time.[18,19] PC cine-MR imaging combined with GRAPPA has rarely been used for coronary flow velocity measurements. In this phantom experiment, V_{max1} in a pixel dimension of 2.40 × 1.67 mm was comparatively accurate when using that sequence, for which patients can generally tolerate one breath-hold, although the TR was set longer for coronary flow velocity measurement compared to other studies using a shared-phase or interpolation technique (approximately 10–20 ms of TR). Thus, PC cine-MR imaging of high spatial resolution combined with GRAPPA using the shared-phase or interpolation technique may be the most useful for accurately measuring coronary flow velocity with sufficiently reduced scanning time in clinical settings.

The most likely explanation for the discrepant flow velocity measurements in earlier studies comparing the two methods is that the studies, which clearly underestimated flow velocity by MRI, applied a large ROI, presumably because of intervoxel averaging or partial volume effect.[13] On the other hand, the studies that showed a better comparison between both measurements most likely applied small ROIs, giving local velocities.[13] We determined the ROIs manually, enclosing the entire lumen within the cross section of the phantom lumen on magnitude images instead of using small ROIs, because this method is clinically the most available to reduce user-dependent technical errors. Furthermore, data analysis software used in our study can determine V_{max1}, which is nearly equivalent to the measurement with small ROIs. During this manipulation, we took sufficient care to avoid inclusion of stationary tissue within the ROIs, such as the vessel wall and surrounding tissue. Therefore, the selection of ROIs was a least significant error source in this study.

Thus, the V_{max1} obtained as in this study is useful at higher spatial resolution for accurate MRI quantification of constant flow velocity. Furthermore, replacement of the widely used breath-hold technique with navigator-guided free-breathing technique during current PC cine-MRI improves flow velocity measurement in coronary arteries by enhancing spatial and temporal resolution. In the future, better receiver coils, faster gradients, and intravascular contrast agents will further enhance flow measurement capabilities.[5] With these improvements, our experimental results may allow remarkably accurate noninvasive measurement of coronary flow velocity and flow velocity reserve by MRI.

Our study has several potential limitations. First, MRI flow velocity measurements may be affected by field inhomogeneity, field eddy currents, radiofrequency effects, and pulse sequence timing.[20] Fortunately, such errors can be minimized by sensitizing flow in only one direction and using altered first gradient moments to measure phase differences.[9] Next, the 6 mm section thickness used in this study is unlikely to affect significantly the through-plane velocity measurement because the imaged plane was positioned accurately perpendicular to the phantom flow direction. Finally, although we generated constant flow circulation in the phantom to reduce the impact of temporal factors on study results, the flow velocity spectrum appeared to

fluctuate slightly from that obtained by the Doppler guidewire method, which can continuously record velocity information throughout the cardiac cycle (>100 samples/s). Thus, the temporally maximum or minimum peak velocities may be missed during MRI data acquisition because of lower temporal resolution (20 samples/s) and be under- or overestimated by MRI. However, this limitation can be insignificant because we compare the temporally averaged measurements by both MRI and Doppler guidewire imaging.

Conclusion

In this phantom experiment using a small tube, MRI measurements of constant flow velocity using a segmented k-space, PC cine-method showed excellent linear correlation with such measurements obtained using intraluminal Doppler guidewire imaging. However, inadequate MRI spatial factors produced significantly underestimated measurements. With MRI, to measure flow velocity accurately and reproducibly it is useful to employ the spatial peak flow velocity of a single pixel within the ROI, enclosing the entire lumen within the cross section of the phantom, in combination with high spatial resolution. Although this MRI technique requires further improvement of spatial and temporal resolution, its refinement may lead to the use of MRI imaging as an accurate, noninvasive modality for evaluating the functional significance of coronary arterial stenoses.

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